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Johan Kjærgaard

Anatomy of the Carotid Glomus and Carotid Glomus-like Bodies (Non-chromaffin Paraganglia)

With Electron Microscopy and Comparison of
Human Foetal Carotid, Aorticopulmonary,
Subclavian, Tympanojugular, and Vagal Glomera

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Translated from the Danish
by
Anna la Cour, née Claessen

Denne afhandling er af det natur- og lægevidenskabelige fakultetsråd ved Odense Universitet antaget til offentlig at forsvare for den medicinske doktorgrad.

Odense Universitet, den 28. juni 1972

B. Harvald,
h. a. dec.



Preface

The studies reported in this volume were carried out in the Anatomy Department of Odense University during the period 1968–1972. The book would never have come into being without the criticism, work, money, time, knowledge, books, spare time, encouragement, ideas, help, thoughts, coffee, material, intellect, understanding, machines, and abilities contributed by Ellen Berg, secretary, Professor Franz Bierring, Vice Chancellor, Anna la Cour, translator, Professor Jørgen Fabricius, M.D., senior physician, Vibeke Sylvest Frederiksen, photographer, Ulla Hauschild-Ottesen, histotechnician, Henning Heide-Jørgensen, senior surgeon, Jesper Hvidberg-Hansen, registrar, Jens J. Jacobsen, senior gynaecologist, Mogens Johansson, draftsman, Lina Jørgensen, secretary, Dina Kjærgaard, Bachelor of Laws, Professor Karl Kristoffersen, M.D., senior gynaecologist, Mrs. Florence Nielsen, Ellen Holm Nielsen, Doctor of Vet. Medicine, Elith Panton, photographer, Elsebeth Ploug, librarian, Palle Sønder, M.D., senior surgeon, and Lise Bech Sørensen, librarian, the Administrative Committee of the Odense Hospital, the Danish Medical Research Council, the Institute Council of the Anatomy Department, the Medical Literature Analysis and Retrieval System, the Odense University Library, the Research Council of Odense University.

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Johan Kjærgaard.

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“... it should be mentioned that the similarity between the carotid body and other nodules such as the tympanic “paraganglion,” intravagal paraganglia, and aortic bodies, has led some (...) to regard the carotid body as merely the largest component of a more extensive system extending from the base of the skull to the heart, and even beyond these limits (orbital “paraganglion,” abdominal vagal paraganglia).” (Adams 1958, pp. 52–53).

Section 1

Introduction

1.1. Definition of Subject.

1.1.1. Definition of the Concept Glomus

The carotid glomus, situated in the carotid bifurcation, has been recognized by anatomists since the middle of the eighteenth century. Within the past four decades several reports have appeared on the occurrence of carotid glomus-like tissue in sites other than the carotid bifurcation. These phenomena have been called by many names: Glomus, gland, ganglion, paraganglion, non-chromaffin paraganglion, and body.

In the present paper the term glomus will be used to designate the carotid glomus and structures described as having the same morphology or function as the carotid glomus or which have been attributed with the ability to develop tumours which cannot be distinguished histopathologically from tumours arising in the carotid glomus. Such tumours will be termed glomus tumours. The following nomenclature will be used for human glomera (cf. Fig. 1.1):

- (A) Carotid glomus: situated in the carotid bifurcation (cf. section 3.1.2).
- (B) Right subclavian glomus: in relation to the root of the right subclavian artery (cf. section 5.1.2).
- (C) Left subclavian glomus: situated at the root of the left subclavian artery or on the anterior left surface of the aortic arch (cf. section 5.1.2).
- (D) Superior aorticopulmonary glomus: in the connective tissue below the aortic arch, superoposteriorly in relation to the ductus arteriosus or the ligamentum arteriosum (cf. section 4.1.2).
- (E) Middle aorticopulmonary glomus: in the connective tissue below the aortic arch, more anteriorly in relation to the bifurcation of the pulmonary trunk (cf. section 4.1.2).
- (F) Inferior aorticopulmonary glomus: as the above, situated in the connective tissue between the aortic arch and the pulmonary arteries, but more caudally, close to the origin of the left coronary artery from the ascending aorta (cf. section 4.1.2).

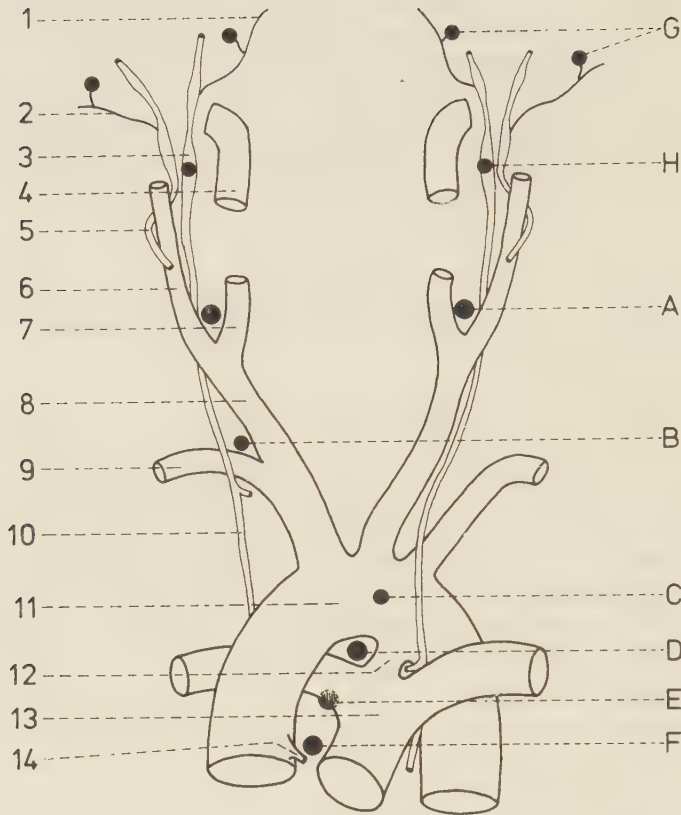


Fig. 1.1. Graphic presentation of the localization of human glomera. A: Carotid glomus. B: Right subclavian glomus. C: Left subclavian glomus. D: Superior aorticopulmonary glomus. E: Middle aorticopulmonary glomus. F: Inferior aorticopulmonary glomus. G: Tympanojugular glomus. H: Vagal glomus. 1: Auricular branch of vagus nerve. 2: Tympanic branch of glossopharyngeal nerve. 3: Inferior ganglion of vagus nerve. 4: Internal jugular vein. 5: Glossopharyngeal nerve. 6: Internal carotid artery. 7: External carotid artery. 8: Common carotid artery. 9: Right subclavian artery. 10: Vagus nerve. 11: Aortic arch. 12: Ductus arteriosus. 13: Pulmonary trunk. 14: Left coronary artery. (Modified after LeCompte 1951).

- (G) Tympanojugular glomus: several small islets of tissue in the temporal bone, partly in the adventitia of the superior bulb of the jugular vein, partly in the tympanic canaliculus, and partly in a submucous situation on the promontory in the tympanic cavity. This glomus occurs along the auricular branch of the vagus nerve (Arnold's nerve) or along the tympanic branch of the glossopharyngeal nerve (Jacobson's nerve) (cf. section 6.1.3).
- (H) Vagal glomus: Embedded in the inferior ganglion of the vagus nerve or in its connective-tissue capsule (cf. section 7.1.2).

Glomus tissue has been observed in several other sites which will be dealt with in Section 8.

1.1.2. Approach to Glomera

Among the named glomera the carotid glomus is exceptional in being the only glomus which is easily discernible at dissection. Indeed, the literature on its development, morphology, physiology, and pathology is comprehensive. Nevertheless, there is not yet agreement on its classification: "There is hardly a single organ in the body of higher mammals studied so much as the carotid body and still any single organ about the structure and function of which we know so little as the carotid body. There is no elucidation especially concerning the connection between the nerve fibres and the glomic cells and the functional relation between the glomic cells and the blood sinuses. These, however, are cardinal questions and extremely important concerning the proper conception of the structure and function of this "mysterious" organ" (Ábrahám 1968a, p. 309).

The other above-mentioned glomera, which owing to their small size will hereafter be referred to as microscopic glomera, have received far less attention in the literature. The vast difference between our knowledge of the carotid glomus and the microscopic glomera may be exemplified by the fact that the fine structural morphology of the carotid glomus is well-known from more than 25 studies on the ordinary experimental animals and 8 studies on a human material, whereas the fine structure of the microscopic glomera has been described only for the subclavian glomus and the aorticopulmonary glomera in experimental animals. From light microscopic studies it is known that glomera exhibit great differences in localization, constancy, and structure from one animal species to the other.

The main objective of the present study was to ascertain whether the carotid glomus-like tissues are so similar to the carotid glomus that this confirms the hypothesis holding that every single of them may be classified as being identical with the carotid glomus. Only a few of the authors who have studied the morphology of the microscopic glomera have compared it with that of the carotid glomus—with the notable exception of Becker (1966a) in his study on aorticopulmonary glomera. To my knowledge there has not previously been any comparative study on the structure of glomus tissue from all localizations performed by a uniform technique on a uniform material.

1.1.3. Object of the Present Study

The present study consists of comparative investigations of human glomus tissue. Its basis is an investigation of the site and structure of the glomic bodies. The main aim was to elucidate, for each microscopic glomus, whether its morphology corresponds to or differs from that of the carotid glomus.

1.1.4. Method of Present Study

The assessment of the glomera was based primarily upon studies of the literature, viz. the descriptions of (1) the ordinary histological appearances, (2) histochemical studies to detect fluorogenic, biogenic amines, (3) the fine structure, (4) the vascular supply, (5) the innervation, and (6) the histogenesis—to the extent that these factors have been elucidated in man and the most common experimental animals. Thorough bibliographies may be found for the carotid glomus in Adams' monograph from 1958 (Adams 1958) and for the aorticopulmonary glomera in Becker's thesis from 1966 (Becker 1966a). With respect to these glomera, therefore, I have based my systematic anatomical description on the recent literature and a selection of the older literature which was considered representative. As far as the other glomera are concerned, I have endeavoured to render, for the human glomera, an exhaustive bibliography of papers published prior to Jan. 1, 1970. As already mentioned, the comparison of the glomera was based upon normal-anatomical criteria. Reports on the physiology and pathology of the glomera are quoted also, when this was considered relevant.

The assessment of the glomera was based, in the second place, upon my own studies, restricted to a description of the glomera on the basis of light microscopic examination of semi-thin sections and electron microscopy of ultra-thin sections of the glomera listed in Fig. 1.1, found by serial sectioning of suited preparations from four human foetuses of a crown-rump length from 55 to 62 mm. The reasons why electron microscopy was chosen as the main method for comparing the glomera were (1) that the conclusions drawn so far have been based upon light microscopic—histological and histochemical—methods, (2) that electron microscopic studies of the carotid glomus have disclosed granules which possibly are of such specific size and fine structure that glomus cells may be identified on the basis of this sole criterion, and (3) that the microscopic glomera in man have not previously been subjected to electron microscopic investigation.

1.2. Attempts at Classifying the Carotid Glomus

1.2.1. Historical

From an historical point of view the beginning of the 1930's marked an epoch in glomus research. Around that time the chemoreceptor properties of the carotid glomus were recognized (cf. section 1.2.6). It was also around and after this period that it became known that tissues in other sites might have certain characteristics in common with the carotid glomus. Accordingly, only a very few of the publications dealing with the microscopic glomera can be considered historic. It seems most natural, therefore, to discuss them in connection with the review of the literature of each individual organ. The older literature on

the carotid glomus has been reviewed by several authors (Adams 1958, Meijling 1937, Murillo-Ferrol 1961, Pick 1959, Villasana 1960, Watzka 1943, White 1935/36). Among these publications I should like to stress in particular those of Pick and Adams (which form the basis of the historical parts of the following six sections). However, in a comparative study of glomic structures with special reference to their classification, I feel it must be relevant to review the classification on the most thoroughly investigated of these organs, the carotid glomus, in the course of time. This review is supposed to serve partly to elaborate the concept glomus tissue, as observed in the carotid glomus, and partly to indicate possibilities of classifying the microscopic glomera.

1.2.2. The Carotid Glomus as an Autonomic Ganglion and as a Modified Autonomic Ganglion

During the period elapsing from the detection of the carotid glomus in the early 1740's (Tavbe 1743) up to the early 1860's, when the only anatomical method of study was dissection, this organ was considered a sympathetic ganglion. The interpretation of this glomus as a small ganglion of little importance is apparent from the Latin terms by which it has been known: Ganglion minutum (Tavbe 1743), ganglion exciguum (Haller 1762), ganglion parvum (Nevbaver 1772), and gangliolum intercaroticum (Andersch 1797). The view that the carotid glomus was a sympathetic ganglion was not attenuated by the fact that in the dissections which disclosed this organ and its connections with the sympathetic trunk as well as in subsequent dissections (Mayer 1833, Svitzer 1863, Valentin 1833) it was discovered that the organ also received fibres from the vagus nerve and the glossopharyngeal nerve.

Despite a very different view of the carotid glomus predominant during the subsequent century, Meijling, in 1937, classified the cells of the carotid glomus as modified, small, peripheral, autonomic ganglion cells. He drew this conclusion after finding in the glomus cells, by nerve staining, neurofibrils and Nissl substance exactly like the corresponding organelles in sympathetic ganglion cells. During the past few years, electron microscopic studies, int. al., have disclosed that the chief cells in the carotid glomus synthesize osmiophilic cytoplasmic granules which possibly contain a neurotransmitter of biogenic amine type, that occasionally the cells develop neuroid processes, and that they are surrounded by neurolemmal cells. Thus, on the basis of structural characteristics it cannot be ruled out that the carotid glomus may be classified as a type among sympathetic autonomic ganglia (Grimley & Glenner 1968).

1.2.3. The Carotid Glomus as an Endocrine Gland of Entodermal Derivation

The first microscopic study of the carotid glomus was performed in 1862 by Luschka. He reported that histologically the organ resembled glandular tissue

and concluded " . . . dass es sich hier überhaupt nicht um ein Ganglion . . . sondern um ein drüsenartiges . . . Organ handelt" (Luschka 1862, p. 406). In accordance with his findings Luschka called the organ the carotid gland and assumed that it had developed from the pharyngeal epithelium. This hypothesis, that the carotid glomus was of entodermal derivation, was supported in 1881, when Stieda published the first paper on the development of the carotid glomus. However, it soon became apparent (Jacoby 1896) that Stieda had confused the glomic primordium with the primordium of the inferior parathyroid gland from the 3rd branchial pouch. That such a mistake had been made was later confirmed (Kohn 1900, Murillo-Ferrol 1967, Rabl 1922, Smith 1924), and since none of the more recent, extremely thorough investigations (Batten 1960, Boyd 1937a, Ito 1950, Murillo-Ferrol 1961, 1967, Rogers 1965) has disclosed the carotid glomus as an entodermal branchiogenic gland, this view must now be considered obsolete.

1.2.4. The Carotid Glomus as a Sympathetic Chromaffin Paraganglion

Truly chromaffin organs, i. e. organs built up of cells with a marked ability to reduce chromates (phaeochromocytes) comprise the adrenal medulla and the organ of Zuckerkandl (Zuckerkandl 1911). In addition, there are islets of chromaffin cells in the ganglia of the sympathetic trunk. Lastly, smaller groups of or solitary chromaffin cells may be scattered in the prevertebral autonomic nervous plexuses and ganglia and along their central and peripheral nerve connections (Boyd 1960, Coupland 1965, Hollinshead 1940a, Watzka 1943).

In the year 1900 Kohn, on the basis of a major histological and embryological study on mammals, claimed that the carotid glomus was homologous to the adrenal medulla, a view which was to exert its influence right up to this day. Kohn stated (1) that the typical cells and ganglion cells in the carotid glomus had been laid down from embryonic sympathetic cells, (2) that already during foetal life the majority of the cells developed distinct chromaffinity, preserved in adult animals, and (3) that the main innervation of the organ—in accordance with the view prevailing in those times—was from the cervical sympathetic trunk. The first-named results were at the time of his study a revolutionary novelty, and Kohn was in his right to ask: "Wie soll dieses Organ nun gedeutet werden?" and "Wie soll man ein solches Organ nennen?" (Kohn 1900, pp. 128 and 129). Owing to the chromaffinity of the specific cells the organ could not be classified as a true ganglion. On the other hand, the carotid glomus was, according to Kohn's own findings, closely related histogenetically and neurogenously to the sympathetic ganglia. He, therefore, suggested setting up a new category of tissue which he designated paraganglia. In accordance with this system, the carotid glomus was termed the intercarotid paraganglion and the adrenal medulla the suprarenal paraganglion. Later, the organ of Zuckerkandl was named the paraganglion aorticum abdominale.

Kohn's analogizing the carotid glomus with the adrenal medulla received physiological support when Mulon, in 1904, produced from the carotid glomus of horses an extract which exerted the same circulatory effect as did extracts from the adrenal medulla. Several contemporary histologists accepted, without reserve, that the carotid glomus was identical with the adrenal medulla (Zucker-kandl 1911). Later, it was established (cf. section 1.2.5, 1.2.6) that Kohn's hypothesis was based upon half truths, so that in order to include also the carotid glomus the concept paraganglion had to be considerably extended.

However, electron microscopic studies have demonstrated that the specific granules in the carotid glomus (Böck, Stockinger & Vyslonzil 1970, Lever, Lewis & Boys 1959) resemble morphologically the catechol amine-containing secretory granules of the adrenal medulla. The granular cells in the carotid glomus receive efferent innervation (Yates, Chen & Duncan 1970). It has been demonstrated by cytochemistry that like the adrenal medulla the carotid glomus contains fluorogenic biogenic amines (cf. section 3.1.5). These findings have given support to the assumption that "... the carotid body may be a gland of internal secretion related to the adrenal medulla and other similar paraganglionic structures" (Karnauchow 1965, p. 1301).

1.2.5. The Carotid Glomus as a Parasympathetic, Nonchromaffin Paraganglion

Before the results of the electron microscopic, histochemical, and fluorescence microscopic studies of the past 10 years were submitted, the four main criteria on which the identity of the carotid glomus with the adrenal medulla were based had already been rejected.

In the first place, it turned out that the greater part of the specific cells in the carotid glomus did not take a brown stain after chromium fixation or at least stained only a faint yellow. Solitary, true chromaffin cells, i. e. cells showing the same staining intensity after chromium fixation as the cells of the adrenal medulla, were found in only a few experimental animals (cf. section 3.1.5). After these findings, the cells or the tissue were called "farblose chromaffine" (Kose 1907), "nicht chromaffine" (Watzka 1930/31, p. 187), or "semilfecromo" (Muratori 1932/33, p. 122).

Secondly, it was discovered that although the carotid glomus did receive cells from the sympathetic nervous system during their development, as demonstrated by Kohn, these cells were secondary (Boyd 1937a, Rabl 1922) to a mesodermal cellular condensation to which neuroblasts from parasympathetic cranial nerves migrated, either along the glossopharyngeal nerve (de Winiwarer 1939) or along the vagus nerve (Benoit 1928) or from both sources (Watzka 1938). According to the last-mentioned authors, the parasympathetic neuroblasts developed into the typical cells of the glomus tissue. Celestino da Costa (1954), however, considered the cellular material from the superior cervical ganglion to be the

main source. He assumed that the sympathogonia from this site were usually so undifferentiated that they did not develop their potential chromaffinity (metaneurogonia).

Thirdly, it was realized that the main innervation of the carotid glomus was not derived from the sympathetic trunk, but from the glossopharyngeal nerve. As mentioned above, the very earliest dissections had disclosed fibres from the glossopharyngeal nerve. One of these studies had even shown that in one case the carotid glomus received exclusively fibres from this nerve (descending branch of the glossopharyngeal nerve, Svitzer 1863, Fig. 2), but this finding remained unheeded throughout the period when the glomus was assumed to be sympathetic. It was not until de Castro, in 1926, demonstrated degeneration of the nerve fibres in the carotid glomus after cutting the glossopharyngeal nerve peripheral to its ganglia, that it was gradually accepted that the sympathetic innervation was less important and inconstant.

Fourthly, it was demonstrated that if extracts from glomus tissue had any circulatory effect at all, such effect was rather depressor, parasympathomimetic (caused by "carotidin", an acetylcholine-like substance?) than pressor, sympathomimetic (Christie 1933a, 1933b, Frugoni 1913). On this basis there gradually developed the hypothesis (Gerard & Billingsley 1923) that the carotid glomus was a parasympathetic, non-chromaffin homologue to the adrenal medulla. In 1930 Watzka introduced the term "nicht chromaffine Paraganglien" to designate the "depressor" paraganglia like the carotid glomus—unlike the "chromaffine, pressorische Paraganglien" such as the adrenal medulla (Watzka 1930/31, p. 189). In addition to purely sympathetic chromaffin and parasympathetic non-chromaffin paraganglia there were also "gemischte" paraganglia in which chromaffin and non-chromaffin types of cell were mixed.

Thereby the concept paraganglia had been extended to designate endocrine, neurogenous organs with efferent innervation, regardless of whether they were derived from the sympathetic or parasympathetic nervous system. The view that glomic tissue is a parasympathetic paraganglion has been maintained in our times by int. al. Watzka and his associates (Kohfahl 1952, Schönberger 1966, 1967, Watzka 1943, Watzka & Scharf 1951).

1.2.6. The Carotid Glomus as a Sensory Paraganglion

In 1926 de Castro had demonstrated degeneration of the nerve fibres in the carotid glomus after cutting the glossopharyngeal nerve peripheral to its ganglia, and had thereby proved that its main innervation was from this nerve. In 1928, he completed this result by anatomical and physiological experiments. Among other things, he cut the roots of the glossopharyngeal nerve central to the ganglia. As the nerves of the carotid glomus did not degenerate after this procedure, he concluded that the perikarya of the nerves were situated in the sensory ganglia of the glossopharyngeal nerve. The conclusion of his anatomical

and physiological experiments was that "Le glomus caroticum n'est pas un paraganglion ni une glande endocrine typique. Il représente bien plutôt un organe sensoriel spécial, destiné peut-être à recueillir certaines modifications qualitatives du sang" (de Castro 1928, p. 378). During the subsequent years de Castro's conclusion received convincing support from physiological findings (de Castro 1926, 1928, Comroe & Schmidt 1938, Heymans & Bouckaert 1933, Heymans, Bouckaert & Dautrebande 1930). The carotid glomus has been characterized physiologically as a specific chemoreceptor whose adequate stimuli consist in a reduction of the arterial P_{O_2} or pH or an increase in arterial P_{CO_2} . Its function and pharmacology have been studied in great detail, *int. al.* by Anichkov, Bouckaert, Heymans, Neil, and Witzleb who have published several reviews (Anichkov & Belen'kii 1963, Heymans 1955, Heymans & Bouckaert 1939, Heymans & Neil 1958, Witzleb 1970).

Several attempts have been made to correlate the physiological findings with the paraganglionic theory. The introduction of the concept sensory paraganglia stands out. In a paper by Pannier, read by Goormaghtigh in 1935, "les paraganglions annexés aux fibres sensitives" are mentioned (Pannier 1935, p. 1352), and after several years' research within this field the specific cells in the carotid glomus were called "sensitive, non-chromaffin paraganglionic cells" (Goormaghtigh & Pattyn 1954, p. 679). In a review concluding 30 years' studies on the glomera along the glossopharyngeal and vagus nerves, Muratori suggested the term "paragangli ad innervazione sensitiva" (Muratori 1960, p. 62).

The most detailed account has been given of the concept "paraganglion sensitif" in Goormaghtigh & Pannier's paper from 1939. These authors, like Watzka (1930/31), distinguished between chromaffin adrenaline-secreting paraganglia having efferent sympathetic innervation, non-chromaffin acetylcholine-secreting paraganglia having efferent parasympathetic innervation, and mixed efferent paraganglia. From this system of efferent paraganglia, however, Goormaghtigh & Pannier separated the carotid glomus and the aorticopulmonary glomera which they classified as sensory paraganglia. Whereas the efferent paraganglia contained ordinary capillaries, the sensory ones were characterized in being made up of arteriovenous anastomoses with myoepithelioid cells of the same type as in the coccygeal glomus and the digital glomera. Apart from the myoepithelioid cells, the sensory paraganglia contained paraganglionic cells most of which were non-chromaffin, only a few being chromaffin. These paraganglionic cells, which possessed the ability to analyse changes in the chemical composition of the blood, were at the same time nervous (derived from the neural crest, provided with satellite cells and axonal processes) and glandular (neurocrine, transmitter-secreting). The cells were in synaptic contact with afferent fibres coursing in the glossopharyngeal nerve (from the carotid glomus) and in the vagus nerve (from the aorticopulmonary glomera).

Hereby, the concept paraganglion had been extended so far that it could capacitate any auxiliary organ to the peripheral nervous system, regardless of

whether the innervation of the paraganglion was efferent or afferent and regardless of whether its embryological and nervous connection with the central nervous system was by way of sympathetic, parasympathetic, or afferent nerves.

1.2.7. The Carotid Glomus as a Myoepithelioid, Arteriovenous Anastomosis of Mesodermal Derivation

Arteriovenous anastomoses have been found in numerous sites (Clara 1956). Well-defined, arteriovenous anastomoses (Staubesand 1951) are collected (1) as digital glomera (syn. cutaneous glomera, Hoyer-Grosser's organ) in the subcutaneous tissue of the finger and toes, especially dense in the nail bed, (2) as the coccygeal glomus (syn. coccygeal body) at the tip of the coccygeal bone in relation to the middle sacral vessels, and (3) as the organs which in mammals are homologous to the coccygeal glomus, viz. the caudal glomera. These organs receive one or more afferent arteries which continue direct in the special glomic canals characterized in being surrounded by modified muscle cells which in the light microscope stand out pale and swollen—epithelioid. These cells have ample innervation by sympathetic fibres. From the rather wide lumina of irregular diameter, surrounded by modified muscle cells, the blood empties direct into efferent veins.

The classification of the carotid glomus as a vascular organ of a type like those mentioned above was first done in opposition to the glandular theory and thereafter to the paraganglionic theory. The arguments against these theories were during one period so weighty that in the Basle nomenclature (*Nomina anatomica* 1895) the structure was designated glomus, a term which has been maintained in the subsequent editions of *Nomina anatomica* (1935, 1955, 1968).

As early as three years after Luschka, in 1862, had introduced the glandular theory, Arnold (1865), on the basis of the morphology of preparations with injected vessels, found that the carotid glomus and the coccygeal glomus were alike and characterized by vascular loops of the "typus der Glomeruli" (Arnold 1865, p. 201). As a consequence, he re-named Luschka's glandula carotica and called it glomeruli arteriosi intercarotici. Arnold's vascular hypothesis was indirectly supported when several embryologists, towards the turn of the century, found that the carotid glomus was of mesodermal derivation, either from the adventitia or from periadventitial cells from the initial portion of the internal and external carotid arteries (Jacoby 1896, Marchand 1891).

In 1938, at a time when the paraganglionic theory was predominant, Schumacher revived the discussion. He found the specific cells in the carotid glomus and in the thoracic glomic structures to be equivalent to the epithelioid cells in the coccygeal glomus, digital glomera, and caudal glomera, and their cells to be invariably myoblastic "epitheloiden Muskelzellen (Quellzellen)" (Schumacher 1938, p. 107).

Present Investigations. Material and Technique

2.1. Material and Technique

The material is derived from four human foetuses designated below by crown-rump length in millimetres: cr 55, cr 59, cr 61, and cr 62.

Table 2.1 gives the foetal age. There is a good correlation between the fertilization age, calculated as 10–11 weeks on the basis of the crown-rump lengths, and the menstrual age stated on the basis of the data given in the records concerning the duration of menostasis and the objective findings at vaginal examination. The foetuses must be assumed to have been normal, as the indication for abortion was in all cases non-eugenic.

Under general anaesthesia the foetuses were removed by laparotomy and hysterotomy (minor caesarean section). The processing was started immediately after the surgeon had enucleated the pregnancy product. A thin needle with a flexible tube (Butterfly-21-G, Abott Laboratories) connected with a syringe was introduced into a cord vessel. Through this vessel 3 % cold glutaraldehyde, buffered with cacodylate to pH 7.4, was injected. The injection of the fixative was done by light manual pressure on the piston. The foetus quickly reacted by generalized muscle contraction. The glutaraldehyde infusion was continued until the produced subcutaneous aldehyde-filled bullae ruptured. The amount of glutaraldehyde used for the initial fixation is shown in Table 2.2. The initial fixation was performed in the operating unit, so that the infusion could be started immediately, i. e. within the first 2 or 3 minutes after the maternal blood supply to the placenta had been interrupted. During the transport from the hospital to the laboratory the foetus was kept in glutaraldehyde in a thermos jug with ice.

Using a Zeiss operation microscope magnifying 6–40 $\times$, I dissected out, as soon as possible, i. e. within three hours, the relevant specimens, cf. Figs. 2.1, 3.1, 5.1, 5.20, and 6.1. During this procedure exposed glomic areas were constantly kept moist with cold glutaraldehyde. The removed specimens were further fixed by immersion into cold buffered glutaraldehyde. Table 2.2 lists the total fixation periods. After aldehyde fixation had been completed, the specimens were rinsed in 0.05 M cacodylate buffer, and after being left, for about 24 hours, in sucrose (except the specimens from foetus cr 59), all were post-fixed for one hour in 1 % osmium tetroxide. The specimens from foetuses cr 55 and 61 were dehydrated in increasing concentrations of ethyl alcohol and carried through propylene oxide to be embedded in Maraglas (Freeman & Spurlock

Table 2.1. Estimated foetal age. Fertilization age given according to Patten (1968), menstrual age according to data from records.

		Foetus			
		cr 55	cr 59	cr 61	cr 62
Fertilization age in weeks.	Crown-rump length ...	10-11	10-11	10-11	10-11
Menstrual age in weeks ..	Duration of menostasis	11 ⁴ / ₇	12 ⁰ / ₇	13 ¹ / ₇	12 ¹ / ₇
	Vaginal examination...	ca. 11 .	ca. 12 .	10-12	12-13

Table 2.2. Details concerning processing of the foetuses and specimens from the foetuses. The table gives only items which differed from foetus to foetus. For general procedure cf. section 2.1.

		Foetus			
		cr 55	cr 59	cr 61	cr 62
Initially injected quantity of glutar-aldehyde, ml		15	15	11	20
Total aldehyde fixation period, hours		24	21	7	22
Left for about 24 hours in sucrose..	Yes	No	No	Yes	Yes
Dehydration medium/intermedium ..	Ethyl alcohol/propylene oxide	Acetone/propylene oxide	Ethyl alcohol/propylene oxide	Acetone/propylene oxide	Acetone/propylene oxide
Embedded in	Maraglas	Araldite	Maraglas	Araldite	Araldite

1962). Specimens from foetuses cr 59 and cr 62 were dehydrated in acetone and carried through propylene oxide to be embedded in Araldite (Sitte 1967).

In a Spencer stereomicroscope (American Optical) equipped with a special illumination device so that the specimens could be viewed in transillumination, it was possible to orient the specimens with the desired side against the block face. The specimens were placed on the flat lid of Beem plastic capsules (No. 00, inner diameter approx. 7 mm) whose pyramid-shaped end, generally used for embedding, had been cut off. The blocks were polymerized for 48 hours at 60° C.

The blocks were trimmed in part manually with a razor blade and in part by a Reichert TM 60 trimming machine. Survey sections and ultrathin sections were prepared on a Reichert OmU2 ultramicrotome mounted with glass knives.

Table 2.3. Material, processing, and findings of glomera. For each glomus area the number of survey sections studied and the mean distance between them are given, as an indication of the degree of processing. For the entire material the mean distance between the survey sections was 10.6 μ m. When considering also that one glomus chief cell is of the same order of magnitude, it will be seen that there was every likelihood of finding any glomera present. However, tissue from the glomus areas was lost in making pyramids for ultramicrotomy. This loss is indicated by the number of pyramids formed. About 0.1 mm was removed around each pyramid. It should be mentioned that within the aorticopulmonary

		Carotid glomus		Area of aortico- pulmon- ary glomus	Area of left sub- clavian glomus	Area of right subcla- vian glomus	Area of tympano- jugular glomus		Area of vagal glo- mus
		R	L				R	L	
Preparations from foetus cr 55	No. of survey sections...			102	61	85	179	94	28
	Mean distance between sections, μm			15.9	12.7	11.5	4.9	12.8	10.1
	No. of ultrapyramids with glomus			3	1	0	1	0	2
	No. of ultrapyramids without glomus			0	2	1	1	2	0
	No. of studied glomera ..	1	1	3	1	0	1	0	2
Preparations from foetus cr 59	No. of survey sections...			169	100	65	110	0 ^a	55
	Mean distance between sections, μm			14.6	13.6	11.0	7.6		7.8
	No. of ultrapyramids with glomus			7	2	0	1		2
	No. of ultrapyramids without glomus			0	0	0	1		0
	No. of studied glomera ..	1	1	3	2	0	1		2
Preparations from foetus cr 61	No. of survey sections...			198	117	65	40	171	22
	Mean distance between sections, μm			14.0	11.3	8.7	10.8	6.8	10.9
	No. of ultrapyramids with glomus			8	1	0	0	0	0
	No. of ultrapyramids without glomus			0	0	4	1	6	1
	No. of studied glomera ..	1 ^b	1	5	1	0	0	0	0
Preparations from foetus cr 62	No. of survey sections...			107	96	85	237	234	37
	Mean distance between sections, μm			13.5	10.9	8.2	8.4	9.7	7.5
	No. of ultrapyramids with glomus			3	3	1	3	3	1
	No. of ultrapyramids without glomus			0	0	0	0	0	0
	No. of studied glomera ..	1	1	3	3	1	3 ^c	3	1

glomus areas from fetuses cr 59 and cr 61 more than one pyramid was formed per glomus. Unlike the other areas, the carotid glomus was not consecutively stepwise sectioned, so that no processing data are given for this glomus. It will be seen that apart from the 8 carotid glomera, another 35 glomera were found. With two exceptions (comments b and c) all the glomera were studied in the electron microscope. Comments: (a) the specimen was damaged during dissection; (b) not ultrasectioned; (c) one of these glomera was not ultrasectioned.

The survey sections studied in the light microscope were $1/2 \mu\text{m}$ thick, stained with basic toluidine blue (Sitte 1967) for 1–2 minutes on a hot plate at about 80° and mounted in Eukitt. Ultrathin sections were collected on supporting copper grids (type R 150 from Zeefplattenfabriek Veco, Eerbeek, Holland) coated with 1.4 % Formvar, and double-contrasted with zinc uranyl acetate 1 % and lead citrate (Venable & Coggeshall 1965). The ultrathin sections were studied and photographed in a JEM-T7 electron microscope (accelerating voltage 60 kV, resolving power about 0.7 nm). When reading the micrographs quantitative measurements were done using a Zeiss particle size analyser TGZ-3 (for further details cf. Appendix II).

To locate the microscopic glomera, blocks containing specimens of these glomera were stepwise sectioned. Each mounted survey section was assessed in the light microscope for content of glomus, and the depth of the next step was based upon this assessment. If a survey section contained cells suspected of being glomus cells a pyramid for ultramicrotomy was trimmed. Table 2.3 gives the number of studied survey sections, the mean distance between these sections, the number of ultrapyramids made, and the number of glomera found.

2.2. Comments on Material and Technique

It is not possible, in theory or in practice, to procure a human biopsy material containing all the glomera that make up the subject of the present study. The only possibility of procuring human material so fresh that the processing does not interfere with the fine structure of the cells is using foetal material from abortions. If such not fully developed individuals are to be well-suited for such an investigation, it is a presupposition that the glomera have been laid down in their permanent site and that they have reached a stage of development at which the fundamental characteristics found in glomus tissue from adults have appeared.

As far as the carotid glomus is concerned, these conditions are fulfilled by foetuses of the ages shown in Table 2.1. The embryogenesis of the glomus tissue has been completed at the 50 mm crown-rump stage. The most important change that takes place during the organogenesis is a relative increase of the stroma (Boyd 1937a, Murillo-Ferrol 1961).

If the hypothesis mentioned in section 1.2 on the identity of the microscopic glomera with the carotid glomus holds, the glomera are homologous in the developmental respect. Consequently, the microscopic glomera are laid down and develop along with the carotid glomus. This assumption was supported by the embryological studies of microscopic glomera (cf. section 5.1.8) which had been published up to 1968–1969, when the present study was planned and the material collected. With respect to the tympanojugular glomus Vara-Thor-

beck, in 1970, reported findings indicating that material from foetuses smaller than c-r 125 mm would be of questionable value (cf. section 6.1.8).

With a view to locating glomera, a foetal material offers advantages above specimens from adults. In adults the glomera, in particular those in the chest (d'Agostini 1959, Boyd 1961, Hughes 1967, Martínez 1939) are disintegrated by connective tissue and therefore difficult to locate.

For electron microscopic study of the glomera the size of the foetus is a definite advantage. As the accurate site of each microscopic glomus varies, a certain amount of tissue has to be searched in order to locate it. For technical reasons specimens for electron microscopy should not measure more than about one millimetre. Specimens of this size from 10–11-week foetuses may contain the structures in relation to which the given glomus is expected to be situated. In addition to the carotid glomus, there is a question of the following glomic areas: (1) base of the heart with the concavity of the aortic arch, the pulmonary arteries, and the ductus arteriosus (Fig. 2.1), (2) the bifurcation of the brachiocephalic trunk (Figs. 2.1, 5.20), (3) the arch of the aorta with the origin of the three great arteries (Figs. 2.1, 5.1), (4) the jugular foramen with adjacent bones (Fig. 6.1), and (5) the interior vagal ganglion.

On the other hand, the small size of the foetuses rendered difficult an accurate gross dissection of uniform, non-traumatized specimens of suitable size. For example, in removing the inferior vagal ganglion it was difficult to avoid damaging the structures passing through the jugular foramen (cf. Fig. 6.16). To restrict this potential damage to specimens containing the tympanojugular glomus area on one side, I removed only one of the inferior vagal ganglia from each foetus.

In dissecting the area of the tympanojugular glomus I used as points of reference the jugular foramen, the hypoglossal canal, and the internal acoustic meatus, aiming at making a frontal section through the opening of the internal acoustic meatus and the hypoglossal canal and sagittal sections 1–2 mm medial to and $\frac{1}{2}$ –1 mm lateral to the jugular foramen. The left specimen from foetus cr 59 was incorrectly cut and was therefore left out of the material.

As far as the thoracic glomera were concerned, I considered that theoretically the ideal glomus areas were those illustrated in Fig. 2.1. In practice, however, it was seldom possible to obtain specimens of the ideal delimitation in the dissection. For instance, major or minor portions of the left subclavian glomus area were always included in the specimen containing the area of the aorticopulmonary glomus (cf. Fig. 5.4).

True, the ideal delimitation was of importance mainly with a view to obtaining an expedient sectioning plane of the individual glomus areas. During the light microscopic examination of the preparations, summarized in Table 2.3, I was always able to decide with reasonable certainty to which of the ideal glomus areas a given section belonged, no matter from which block it was derived.

Thus, the difficulty in dissecting from the pre-fixed foetuses did not consist

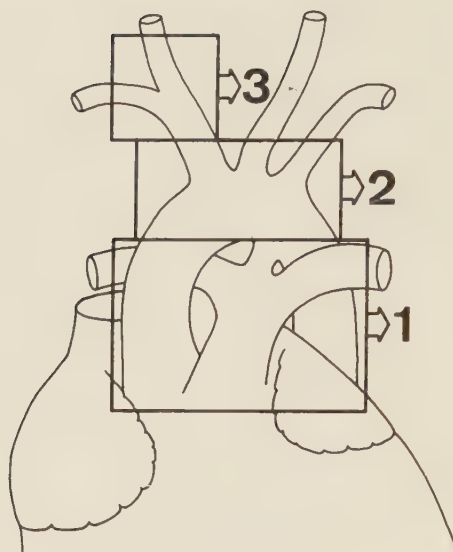


Fig. 2.1. Diagram of the ideal glomus areas in the chest. The area of the aorticopulmonary glomus (1) comprising vessels and nerves between two horizontal planes in the mediastinum, one through the base of the heart and one through the most cranial point in the concavity of the aortic arch; the area of the left subclavian glomus (2) comprising vessels and nerves (except the phrenic nerves) between two horizontal planes in the mediastinum, one through the most cranial point in the concavity of the aortic arch and one about 1 mm cranial to the most cranial point in the convexity of the aortic arch; the area of the right subclavian glomus (3) comprising the bifurcation of the brachiocephalic trunk with surrounding nerves.

in orientation, but in dissecting the specimens correctly with a margin which was only fractions of a millimeter. When the specimens were to be embedded, the situation had altered; now there were difficulties of orientation in the structures in the osmium-fixed, epoxy resin-imbibed specimens detached from their surroundings. An aid in orientation was inspecting the preparations in strong transillumination (Figs. 3.1, 5.1, 5.20, 6.1). But even by this technique it was not possible to attain a reliable orientation in the area of the aorticopulmonary glomus. For example, it was found in the stepwise sectioning that the aorticopulmonary glomus area from foetus cr 62 had been embedded in fact for frontal sections, although the optimal sectioning plane was transverse.

In planning the plane of sectioning and thus the position of embedding, I took the following considerations into account: (1) The surface of the specimen that was lying against the lid of the Beem capsule had to be suitably plane and large for the specimen to preserve its position during the phase of polymerization. (2) In the stepwise sectioning it was to be possible, after a few survey sections, to identify the structures in the preparation. It was helpful in

the identification that the epoxy resin blocks were partially transparent, so that when viewing the entire block under the stereomicroscope in transillumination or in incident light I could occasionally elucidate the embedded structures. (3) The occurrence of two glomera in the same survey section had to be avoided, as this would reduce the possibility of making ultrathin sections of both. The making of an ultrapyramid containing one glomus might necessitate cutting the other one off. (4) The time-consuming procedure of performing stepwise sectioning of epoxy resin blocks rendered it necessary to bear in mind that a given glomus area could be thoroughly studied by viewing the fewest possible number of survey sections.

Despite the small size of the anatomical structures in 10–11-week fetuses the specimens of the aorticopulmonary glomus and the tympanojugular glomus areas were considerably larger than required by the ideal demands on an electron microscopic preparation, being $6 \times 6 \times 5$ mm. Even after the necessary large area trimming, it was necessary, in order to locate the glomera, to make several hundreds of epoxy resin sections measuring 20–25 mm². Owing to the special demands of the task, I had to renounce technical perfection.

The technique of consecutive stepwise sectioning of epoxy resin blocks also had the drawback that a good deal of tissue from the embedded preparation was lost when the block was trimmed, in particular when pyramids for ultramicrotomy were made. The number of ultrapyramids made may be seen from Table 2.3 from which it is apparent, by adding the columns that (when disregarding the carotid glomus) a total of 61 ultrapyramids were trimmed. It is apparent also that in 19 cases ultrathin sections were cut from cells which on electron microscopy could not be considered glomus. These were (1) questionable or fairly unassessable findings (cf. section 6.3), (2) Schwann's cells, (3) small ganglion cells, and (4) mesenchymal cells, in particular tangentially cut small vessels in formations unfortunate from the differential diagnostic point of view.

The tissue removed from the block in the ultrapyramid trimming could not be investigated for content of glomera. So that as little as possible of the tissue from the glomus areas would be lost, the ultrapyramids were made very low and flat. When the specimens from fetuses cr 59 and 62 were being processed the laboratory had a Reichert TM 60 trimming apparatus available for testing. For this apparatus special small-calibre milling cutters were made in the Laboratory and so was a specimen holder which allowed great mobility of the block in the plane of the block face. By this equipment I could, on finding a glomus-suspected area in a block, cut off under controlled conditions the surrounding tissue in planes parallel to the block face. In this way there was attained on the block a rectangular prism about 0.1 mm in height. The prism could then be hand-trimmed to the shape of an ultrapyramid. When using these partly machine-made ultrapyramids (Fig. 2.2) far less tissue was lost than on hand-trimming with a razor blade.

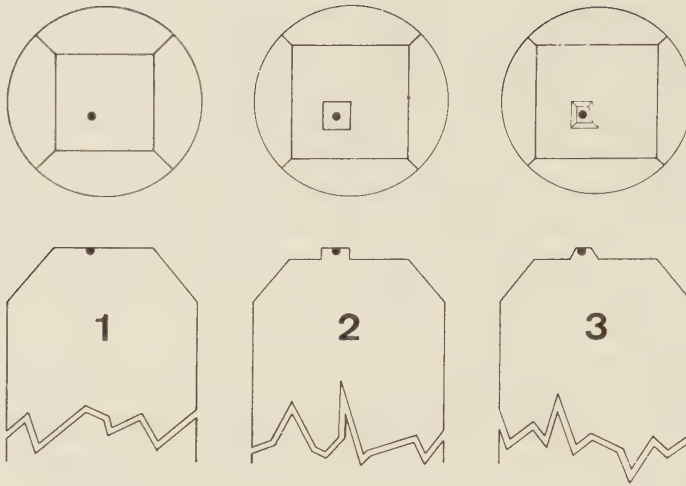


Fig. 2.2. Partly machine-made ultrapyramid. Diagram showing procedure with a block exhibiting the situation (1) on finding a glomus in the survey section, (2) after milling about 0.1 mm off the block in a plane parallel to the sectioning plane, and (3) after the resulting glomus-containing prism has been trimmed by a razor blade to the shape of a pyramid frustum having a sectioning surface of approx. 0.5×0.6 mm.



Fig. 2.3. Processing of ultrapyramids around two glomera found in the same survey section. Diagram showing procedure with a block exhibiting the situation (1) on finding two glomera in the same survey section, (2) after tilting the block to a pre-calculated, suitable angle, so that on further sectioning the glomus on the right re-appears in the survey sections without (3) it being necessary to remove the glomus on the left in making a partly machine-made ultrapyramid around the right glomus; (4) after ultrasectioning and continued stepwise sectioning and back-tilting of the block to the original angle, and (5) after making a partly machine-processed ultrapyramid around the left glomus.

Owing to the possibility of pre-calculating the loss of tissue in making the ultrapyramids I was able to make ultrathin sections of two glomera found in the same survey section (cf. Fig. 2.3). This technique was of decisive importance in processing the aorticopulmonary area from foetus cr 62 which had been embedded in an unfortunate position.

From the point of view of ultrasectioning neither the flat hand-cut nor the

partly machine-made ultrapyramids were optimal. As my description of the fine structure is based upon low power and medium power views (original magnification from 1,500 to 30,000 $\times$), silver and pale gold coloured sections were sufficient.

In comparing the glomera it would have been ideal, if the foetuses had been of exactly the same age. Thereby developmental variations in appearance would be restricted as far as at all possible. Moreover, if all glomera were treated by the same technique, technically-conditioned variations in their appearance would be restricted as far as possible. These ideal demands on material and technique were not fulfilled. Table 2.2 illustrates the differences between the foetuses and their preparation. It is an unfortunate difference in the processing of the material that the preparations were not dehydrated and embedded in identical media. The embedding medium had to be changed because one member of the laboratory staff developed hypersensitivity symptoms.

When considering glomera from the same foetus the ideal demands for comparison are fulfilled, provided that the fixative, dehydration, and embedding media have had the same possibilities of contact with the glomera. The possibility that the fixative has of influencing the glomera is considered crucial. As the dissection took hours, pre-fixation of the glomera *in situ* had to be done. It was performed by injecting aldehyde into the foetal vascular system. From my sections for light microscopy I know that the lumina of the large vessels—arteries as well as veins—such as the aortic arch and its branches to the head and upper limbs, pulmonary arteries, and internal jugular vein, were always empty of blood cells. Smaller vessels were often filled with blood cells. The fact that the large arteries as well as the veins had been flushed free of blood is due to the arteriovenous shunts in the foetal circulation: On injection through the cord vein the injection pressure in the right atrium will be transmitted by way of the foramen ovale to the left atrium.

Owing to the obstruction of a number of the small vessels it might be expected that the glomera supplied by relatively large vessels (aorticopulmonary glomera, carotid glomus) were well-fixed, whereas glomera supplied by small vessels (e.g. the vagal and the tympanojugular glomera) would be less well-fixed. That this was not so may be due to the fixative effect having been less of a “perfusion” of the organs than an “immersion” of the organs in the relatively large pool of fixative which accumulated in the great vessels in whose immediate vicinity all the glomera were situated.

As already mentioned there was a considerable difference between the size of specimens of the glomus areas. A specimen of the inferior vagal ganglion was about 0.3 mm thick, specimens of a tympanojugular glomus or aorticopulmonary glomus area 4–5 mm thick. This latter thickness by far exceeds the size which is critical with a view to proper osmium fixation.

All the glomera found were less than 1 mm from a large vascular lumen which was, during the fixation by immersion, as well as during the phases of

dehydration and embedding, in free communication with the surrounding fluid. Thus, the route of diffusion between the vascular lumina and the glomera was short, irrespective of the fact that the glomus made up only a very small part of a large specimen. A facilitating factor is that the loose embryonic mesenchyme must be assumed to make up a poor diffusion barrier compared with firm collagen connective tissue.

Carotid Glomus

3.1. Review of the Literature

3.1.1. Synonyms for Carotid Glomus

Early nomenclature, cf. section 1.2.2.

Ganglion intercaroticum (Latin: Mayer 1833).

Glandula carotica (Latin: Luschka 1862).

Glomeruli arteriosi intercarotici (Latin: Arnold 1865).

Nodulus caroticus (Latin: Marchand 1891).

Glomus caroticum (Latin: Nomina anatomica 1895).

Paraganglion intercaroticum (Latin: Kohn 1900).

Paraganglion caroticum (Latin: Kose 1907).

Carotid body (The term most commonly used in recent Anglo-Saxon literature).

3.1.2. Site and Size

Thorough dissections of the carotid bifurcation to elucidate the carotid glomus have been performed in recent times by White (1935/36), Engström, Hamberger, Holmer & Rignell (1957), and by Heath, Edwards & Harris (1970). The carotid glomus was situated, shifted a bit medially, in the carotid bifurcation. It was ovoid in shape, its long axis parallel to the common carotid artery. Quite often it was divided into two parts, connected by an isthmus, or entirely separated. The organ was found to be lying in loose connective tissue containing ample fat. At its caudal pole, however, it was connected by a fibrous connective-tissue strand, Mayer's ligament (Mayer 1833), to the medial part of the bottom of the bifurcation. Its colour was reddish-brown, its consistency firm, and its surface viewed in a hand lens slightly nodular.

On micrometry of serially sectioned preparations of both carotid glomera from 21 individuals Heath, Edwards & Harris (1970) found the mean of the maximum diameters to be 3.3 (standard deviation 1.0) $\times$ 2.2 (standard deviation 0.6) $\times$ 1.7 (standard deviation 0.5) mm. Its weight in an autopsy series of 40 adults averaged 12.9 mg for the right and 11.3 mg for the left carotid glomus. The mean weight of both glomera from the same individual was 24.2 mg. The maximum and minimum weight of each glomus was 47.4 and 1.9 mg. Martínez (1939), measuring the carotid glomus from 51 adults aged 16—

100 years, found an average of $3 \times 1.4 \times 1.5$ mm. The largest organ was $5 \times 2 \times 2$ mm and the smallest $1 \times 0.5 \times 0.5$ mm. On vivisection on cats the size of the carotid glomus during extreme hypercapnia was only a fraction of its size during normal ventilation, and it increased in size during hyperventilation with oxygen (de Castro 1951).

3.1.3. Light Microscopic Structure

Microscopically the carotid glomus in adults (White 1935/36, and others) was found to be characterized by a stroma containing both vessels and nerves. The organ was surrounded by a capsule of firm collagen connective tissue. This capsule was traversed by vessels and nerves, but there was no true hilus. The explanation is presumably that the capsule was penetrated in two sites, by nerves and veins at the upper pole and by arteries at the lower. From the inside of the capsule there departed strong connective-tissue septa dividing the organ into about 20 lobes. Each lobe was subdivided by thinner septa into about 5 lobules (glomeruli). These septa were made up of loose collagen connective tissue with a few elastic fibres. The lobulation of the organ set in during the 3rd–4th foetal month. At birth the organ was still predominantly parenchymal, and with advancing age the connective-tissue content increased appreciably (Boyd 1937a). In elderly persons the carotid glomus was cirrhotic with isolated, scattered lobules (Martínez 1939).

In experimental animals a distinction was made, according to the amount of connective tissue, between two histological types, a compact type in which the cellular nests were dense, e. g. in the cat and rat (Muratori 1962b, White 1935/36), and a diffuse type in which the cellular nests were scattered over a larger area, e. g. in the rabbit (Muratori 1962b). An intermediate type was observed in pigs (Muratori 1962b).

In each lobule the parenchymal cells formed whorls and strands in intimate relation to numerous nerves and thin-walled vessels. Modern descriptions of the light-microscopic structure of the parenchyma, confirmed by electron microscopy, are derived chiefly from the studies of de Castro (1926, 1928, 1929, 1940, 1944, 1951, 1962). Hollinshead (1940a, 1943), de Kock (1954, 1960), who studied animals, and Heath, Edwards & Harris (1970), Langer (1952), and Grimley & Glenner (1967, 1968) who described the human carotid glomus. The last-mentioned authors used semi-thin plastic sections. According to these descriptions a distinction is made between the following, constantly present cell types in the lobules:

(1) Chief cells = glomus cells*, specific cells, epithelioid cells, glomus cells type

*) The term glomus cells will be used in the present paper as a collective term for chief cells and supporting cells, especially in cases where a definite distinction is difficult.

I (de Kock 1954), enclosed cells, incapsulated cells, chemoreceptor cells, main cells, lobular cells (Fine, Enriquez & Morales 1968), receptor cells (Niedorf, Rode & Blümcke 1970).

(2) Supporting cells = sustentacular cells, capsule cells, satellite cells, glomus cells type II (de Kock 1954) enclosing cells, incapsulating cells, surrounding cells, sheet cells, perilobular cells, (Fine, Enriquez & Morales 1968), pericytes (Lever, Lewis & Boyd 1959, Palkama 1965).

(3) Pericytes (de Castro & Rubio 1968, Grimley & Glenner 1967) = reticuloendothelial cells (de Kock 1960, de Kock & Dunn 1966), littoral cells (Hoffman & Birrell 1958), periendothelial cells (Al-Lami & Murray 1968a).

(4) Endothelial cells.

(5) Schwann cells with nerve fibres (de Castro 1951, de Kock & Dunn 1966).

Other types did occur, but their presence was not constant and they were situated predominantly in the connective tissue between the lobules. Ganglion cells were found in animals (Al-Lami & Murray 1968a, Biscoe & Stehbens 1966, de Castro 1926, Hoffman & Birrell 1958, Martínez 1939, Meijling 1937) and in man (Boyd 1937a, de Kock 1954). Pryse-Davies, Dawson & Westbury (1964) found ganglion cells in 25 out of 32 human carotid glomera. Occasionally lymphocytes, plasma cells, mast cells, and macrophages were encountered (Ehrenbrand 1964, Fería-Velasco & González-Angulo 1968). The occurrence of true chromaffin cells will be discussed in section 3.1.5.

A definite distinction between chief cells and supporting cells was obtained by de Kock (1954) by means of Holmes' silver staining. However, in retrospect, it is probable that earlier authors too have observed the supporting cells (Goor-maghtigh & Pannier 1939, Meijling 1937, White 1935/36). In the light microscope the chief cells presented themselves as 10–15 μm large polygonal cells (Grimley & Glenner 1967, Heath, Edwards & Harris 1970, Martínez 1939) with pale nuclei, about 7 μm , of a loose chromatin structure, bounded by a distinct nuclear membrane. The cytoplasm was ample, pale, slightly eosinophilic, granulated, with a few vacuoles. The cell borders were poorly defined. In light microscopy of semi-thin plastic sections Grimley & Glenner (1968) were able to distinguish between chief cells with a pale and with a dark hyaloplasm. The nuclei of the supporting cells were about half as large as those of the chief cells and were about 6 times less common (de Kock 1954). According to Heath, Edward & Harris the supporting cells made up about 40 % of the total number of parenchymal cells in man. The nuclei were irregular in shape and chromatin dense. The cytoplasm was scanty with discrete processes. The pericytes were described by de Kock (1960), who studied the carotid glomus after intravital staining. She found that a few cells, larger than the endothelial cells, took up a very small quantity of dye. On electron microscopy (Grimley & Glenner 1967, Hoffman & Birrell 1958, de Kock & Dunn 1966, Lever, Lewis & Boyd 1959) these cells were found to be of a perivascular situation, not—as first assumed—forming part of the endothelial layer.

3.1.4. *Electron Microscopic Structure*

The first brief descriptions of the electron microscopic appearance of the carotid glomus were published in 1957 (Engström, Hamberger, Holmer & Rignell 1957, Lever & Boyd 1957, Ross 1957a). Since then a large number of descriptions have dealt with this organ int. al. in the cat, rat, mouse, hamster, guinea pig, rabbit, dog, horse, and monkey (Al-Lami & Murray 1968a, 1968b, Battaglia 1966, 1968, 1970, Biscoe, Lall & Sampson 1970, Bisco & Stehbins 1966, 1967, Blümcke, Niedorf & Rode 1967, Blümcke, Rode & Niedorf 1967, de Castro & Rubio 1968, Chen & Yates 1969, Chen, Yates & Duncan 1969, Duncan & Yates 1967, Garner & Duncan 1958, Hess 1968, Hoffman & Birrell 1958, Höglund 1967, Kobayashi 1968, Kobayashi & Uehara 1970, de Kock & Dunn 1966, 1968, Kraus & Martínek 1967, 1968, 1970, Lever, Lewis & Boyd 1959, Morita, Chiocchio & Tramezzani 1969, Niedorf, Rode & Blümcke 1970, Palakama 1965, Ross 1959, 1967, Yates, Chen & Duncan 1970, Zapata, Hess, Bliss & Eyzaguirre 1969).

After Nakayama (1961) introduced glomectomy in the treatment of bronchial asthma several laboratories have obtained relatively well-suited human operation material for electron microscopic investigation (Ábrahám 1969, Böck 1970c, Böck, Stockinger & Vyslonzil 1970, Grimley & Glenner 1967, 1968, Kraus & Martínek 1967, 1968, 1970, Simárszky & Lapis 1970). Fería-Velasco and his associates (Feria-Velasco & González-Angulo 1968, Fería-Velasco, González-Angulo & Zavala 1966) studied human carotid glomera from a not particularly well-suited autopsy material that was 1–2 hours old. Battaglia (1969) studied carotid glomera from two human two-month old perfusion-fixed fetuses.

Where the general fine structural characteristics are concerned there is a surprising conformity between the results of these numerous investigations. The differences that exist may be explained as follows: (1) The earliest studies were done by techniques as yet not fully developed. (2) Different methods have been used, in particular different fixatives. (3) Differences between the animal species which were known also from the light microscopic studies. (4) Some of the studies were done for very special purposes, e. g. studying the effect of anoxia, experiments on nerve degeneration, and autoradiographic studies.

Details of the fine structure are given in the thorough descriptions by Ábrahám (1969) and Grimley & Glenner (1968) and in the present investigation and discussion (sections 3.2, 3.3), and here only the following main features will be given in outline on the basis of the review of the literature: The chief cells were oval and had processes. The cells contained numerous organelles, including specific membrane-bounded osmiophilic granules, mean diameter 130 nm (Grimley & Glenner 1968). The cytoplasm presented with varying electron opacity. The chief cells were surrounded by supporting cells and cytoplasmic extensions from supporting cells. Numerous nerves and nerve endings were observed in relation

to the cells. The nerve fibres were embedded in Schwann cells whose function was taken over by the parenchymal supporting cells which, also through mesaxons carried the nerve fibres to the chief cells. Collagen fibres were interposed between nests of chief cells and supporting cells. Unlike light microscopy, electron microscopy disclosed that there was never, or rarely, immediate contact between the chief cells and the vascular endothelium. The vessels were surrounded by a basal lamina, the chief cells by supporting cells with their basal lamina. Between the basal laminae around the vessels and supporting cells there was interposed a perivascular space containing collagen fibres and pericytes.

3.1.5. *Biogenic Amines*

Comprehensive cytological and histochemical studies of the carotid glomus have been performed by Becker and his colleagues (Becker 1966a, Becker, Drukker & Meijer 1967), Fine, Enriquez & Morales (1968), Hollinshead (1943), Lever, Lewis & Boyd (1959), Pryse-Davies, Dawson & Westbury (1964), and Ross (1957b). In comparing the carotid glomus with the microscopic glomera investigations of the following biogenic amines are of most interest: catechol amines (adrenaline, noradrenaline, and dopamine) and 5-hydroxytryptamine (= serotonin = enteramine = enterochromaffin).

The most specific method for demonstrating these biogenic amines is formaldehyde-induced fluorescence. Although it has not yet been elucidated which of the biogenic amines predominate, it was demonstrated by this method that they were present in the carotid glomus of rabbits, rats, cats, pigs, and calves (Becker, Drukker & Meijer 1967, Blümcke, Rode & Niedorf 1967, Dearnaley, Fillenz & Woods 1968, Muratori, Chiarini & Battaglia 1966, Muscholl, Rahn & Watzka 1960, Niedorf, Rode & Blümcke 1970, Palkama 1965, Rahn 1961, Rees 1967) and in man (Hamberger, Ritzén & Wersäll 1966, Niemi & Ojala 1964). Extraction and chromatographic or fluorometric analysis also revealed biogenic amines (Chiocchio, Biscardi & Tramezzani 1967, Dearnaley, Fillenz & Woods 1968, Muscholl, Rahn & Watzka 1960, Rahn 1961). By autoradiography it was demonstrated in rats, mice, and hamsters that the carotid glomus took up precursors of catechol amines (3,4 dihydroxyphenylalanine) and of 5-hydroxytryptamine (5-hydroxytryptophane) (Chen & Yates 1969, Gershon & Ross 1966, Helpap & Hempel 1968). On electron microscopic autoradiography more than half the activity was found to be localized where the specific granules were concentrated (Chen & Yates 1969). Following administration of reserpine, which has a catechol amine-liberating effect upon the adrenal medulla, the number of specific granules in the carotid glomus dropped or their density decreased (Chen & Yates 1969, Chen, Yates & Duncan 1969, Lever, Lewis & Boyd 1959, Niedorf, Rode & Blümcke 1970). By cytochemical methods (modifications of those used by Tramezzani, Chiocchio & Wassermann 1964, Wood & Barnett

1964) it was also rendered likely in electron microscopy that biogenic amines had accumulated in the osmiophilic granules of the chief cells (Battaglia 1968, 1969, 1970, Chen, Yates & Duncan 1969, Chiochio, Biscardi & Tramezzani 1967, Muratori, Battaglia & Modonesi 1965a, 1965b).

Classical methods for demonstrating the biogenic amines utilize the ability of these substances to reduce metals. The iodaffin reaction was positive in pigs (Muratori 1962b, Rahn 1961) and calves (Muscholl, Rahn & Watzka 1960, Rahn 1961). In cats and rabbits Muratori (1962b) found no iodaffin cells, whereas Priimak (1960) reported a positive reaction in a number of cells. In dogs (Serafini-Fracassini & Frasson 1966) the reaction was negative. The cells in the carotid glomus were not or at least only very slightly argentaffin (Becker 1966a, Lever, Lewis & Boyd 1959, Pryse-Davies, Dawson & Westbury 1964, Rahn 1961). On the other hand, the chief cells in experimental animals (de Kock 1954, Lever, Lewis & Boyd 1959, Ross 1957b) as well as in man (Willis & Tange 1959) were strongly argyrophilic. However, this is at variance with Becker's material (Becker 1966a).

In assessing the most commonly used method for metal reduction, the chromaffin reaction, it must be taken into account not only that like other metal reductions the method is non-specific, but also that the reduction is erratic. It depends upon the solution of chromate used, its pH, and upon the time elapsing from the removal of the tissue until fixation is commenced (Lever, Lewis & Boyd 1959). When these factors are borne in mind, the review of the literature on the chromaffinity of the carotid glomus raises two questions.

The first question is whether the chief cells are chromaffin. As mentioned in section 1.2.4 the carotid glomus was believed, around the turn of the century, to be a truly chromaffin organ. Most subsequent investigators have found that the main part of the cells in the carotid glomus, in man (Becker 1966a, Boyd 1937a, Langer 1952, Pryse-Davies, Dawson & Westbury 1964) as well as in a large number of mammals (Becker 1966a, Boyd 1937a, de Castro 1926, Goormaghtigh & Pannier 1939, Hollinshead 1943, Langer 1952, Lever, Lewis & Boyd 1959, Palkama 1965, Penitschka 1931, Priimak 1960, Rahn 1961, Rogers 1965, Ross 1957b, Smith 1924, White 1935/36) were not chromaffin in the strict sense of the word. To-day, with the use of the above-mentioned, far more specific methods, there is no longer any doubt that the carotid glomus contains biogenic amines (although not in the same quantity or in the same mutual proportions as in the truly chromaffin cells). This explains why several of the earlier authors found that a varying porportion of the cells assumed a yellow or pale yellowish-brown tinge after chrome fixation, in man (Boyd 1937a) as well as in animals (de Castro 1926, Hollinshead 1943, Lever, Lewis & Boyd 1959, Priimak 1960, Ross 1957b). On this basis I feel justified in characterizing the chief cells in the carotid glomus as semichromaffin. (The term pseudo-chromaffin suggests that the reaction is false, i. e. not induced by biogenic amines, and according to what has just been said this is not so).

The other question is whether a few true chromaffin cells do occur in the carotid glomus. They have been found in pigs (Boyd 1937a, Rahn 1961), cows (Rahn 1961, Smith 1924), young rabbits (Priimak 1960), cats (de Castro 1944, Goormaghtigh & Pannier 1939, Langer 1952, Priimak 1960, Smith 1924), and dogs (Kobayashi 1968). In the carotid glomus of the cat de Castro & Rubio (1968) and Morita, Chiocchio & Tramezzani (1969) have found cells having the same fine structure as the cells of the adrenal medulla. When considering also that the carotid glomus receives sympathetic nerves and that genuine chromaffin cells may occur along all such nerves, they may be expected to occur in the carotid glomus as an inconstant, non-integrating component of this organ (Boyd 1960, Hollinshead 1943).

3.1.6. Vascular Supply

The carotid glomus in man was found to be supplied by one, two, or more arteries having their origin in the internal carotid artery a few millimetres cranial to the carotid bifurcation, from the bifurcation itself (de Castro 1951, Martínez 1939, White 1935/36), or from the ascending pharyngeal artery (Boyd 1937a). The arteries ascended to the caudal pole of the carotid glomus. Within its capsule they branched into interlobular arteries and arterioles. Each lobule was supplied by one arteriole (de Castro & Rubio 1968, White 1935/36). The venous drainage was according to the lobular pattern, but unlike the arteries the vein traversed the capsule at the upper pole, forming around it a venous plexus (Murillo-Ferrol 1961). From this plexus ran a vein, constantly present, called the intercarotid pharyngeal vein. It ascended a few centimetres between the carotids and emptied into the pharyngeal plexus or other afferents to the internal jugular vein (Murillo-Ferrol & González-Santander 1962). In experimental animals (dogs, rabbits, and cats) the blood ran from the carotid glomus either to the internal jugular, to the external jugular, or to both jugular veins (Chungcharoen, de Burgh Daly & Schweitzer 1952, Niedorf 1970).

The intralobular vessels have been thoroughly studied, *int. al.* by injections, by de Castro (1962) and de Castro & Rubio (1968) who distinguished between three types of vessel. Firstly sinusoids (type I capillaries), secondly ordinary capillaries (type II capillaries), and thirdly narrow postcapillary canals. The sinusoids, numerically predominant, formed the direct continuation of the arterioles. They were tortuous, anastomosing, and had lumina varying in width from 14 to 28 μm . Before the blood from this meshwork emptied into the venules it passed from the sinusoids through very narrow postcapillary canals with a lumen of less than 6 μm . Ordinary capillaries with lumina of 6–12 μm were scarce; they formed anastomoses between the sinusoids.

In addition, the vessels of the carotid glomus have been found to exhibit other special features: (1) Arteriovenous anastomoses (de Castro 1940, 1951, 1962, de Castro & Rubio 1968, Serafini-Fracassini & Volpin 1966). The major-

rity of arteriovenous anastomoses were in or immediately beneath the capsule. The vessels making up the anastomoses were built up of a thick intima, consisting of myoepithelioid cells, a thin media of circularly arranged smooth muscle cells, and a thick adventitia. (2) Baroreceptive innervation (de Castro 1926, 1928, 1940, 1951, de Castro & Rubio 1968, de Kock 1954). The main arteries to the carotid glomus, like the vessels of the arteriovenous anastomoses, had a thin media of smooth muscle cells and a thick adventitia. The thick adventitia in the arteriovenous anastomoses and in the main arteries was supplied with baroreceptive nerve endings. (3) During development a change in the origin of the main arteries took place (Boyd 1937a, Ito 1950). In human embryos less than about 26 mm in crown-rump length the carotid glomus primordium was supplied by a small artery originating in the internal carotid artery. After retrogression of this artery the organ was supplied by the external carotid or its ramifications (Boyd 1937a).

3.1.7. Nerve Supply

Several methods have been utilized in the attempt to elucidate the innervation. Dissection studies very soon disclosed (cf. section 1.2.2) fibres to the carotid glomus from the sympathetic trunk, glossopharyngeal nerve, and vagus nerve, but owing to the small calibre of the nerves and their mutual anastomosing the method led the early investigators astray, making them believe that the organ had predominantly sympathetic innervation. Dissection combined with microscopic examination (Gerard & Billingsley 1923) revealed that the majority of the fibres from the superior cervical ganglion to the carotid bifurcation were not to the glomus, but to the vessel walls.

Dissecting 58 normal human adult cadavers Boyd (1937b) constantly found a branch from the glossopharyngeal nerve to the carotid bifurcation. In the official nomenclature of to-day this nerve is called the *ramus sinus carotici n. glossopharyngei* (Nomina anatomica 1968), but is most often known merely as the sinus nerve. In Boyd's material its origin was most commonly 2–3 cm below the base of the skull, having two roots which united in a trunk running caudally on the lateral aspect of the internal carotid artery. During its course the sinus nerve anastomosed in 40 cases with the vagus nerve (ramifications from the pharyngeal branch, superior laryngeal nerve, or the main trunk of the vagus nerve), in 18 cases with the sympathetic trunk, and in 3 cases with the hypoglossal nerve. Dissection under a hand lens showed that in most cases the nerve terminated in an intercarotid plexus.

A good method for deciding whence the nerves to the carotid bifurcation are derived is histological examination of embryos and foetuses. In prenatal cats de Castro (1940) found, apart from the sinus nerve, also branches from the superior laryngeal nerve and from the superior cervical ganglion. From the same sources a nerve plexus formed in the carotid glomus of prenatal dogs

(Nielsen 1968). Boyd (1937a) found in his human embryo-foetal material a plexus formed from the glossopharyngeal nerve (carotid sinus branch and ramifications from the pharyngeal branch), from the vagus (ramifications from the pharyngeal branch and from the superior laryngeal nerve), and from the sympathetic trunk. When paying regard to the species variations that have to be expected (Ábrahám 1968b), the above-mentioned results accord with those of others (Benoit 1928, Ito 1950, Murillo-Ferrol 1961, Rogers 1965, Smith 1924, Watzka 1938).

By degeneration experiments combined with light microscopy (de Castro 1926), it was ascertained that the main innervation of the carotid glomus was from the glossopharyngeal nerve and that these fibres were afferent (de Castro 1928). In similar experiments Muratori (1932/33) demonstrated that this also applied to the vagus fibres in chicks.

It was demonstrated also, by degeneration experiments combined with electron microscopy, that the sympathetic fibres were not in contact with the glomus chief cells (Lever, Lewis & Boyd 1959, Ross 1967), but with the glomus vessels (Biscoe & Stehbens 1967, Rees 1967). Extracranial cutting of the glossopharyngeal fibres caused degeneration of a large number of nerve fibres in contact with the chief cells (Biscoe & Stehbens 1967, de Castro & Rubio 1968, Hess 1968, Ross 1967). According to de Castro & Rubio (1968) intracranial cutting of the glossopharyngeal roots did not lead to degeneration of the nerve endings, whereas Biscoe, Lall & Sampson (1970) observed that endings of efferent type (cf. section 3.3) degenerated after this procedure. This latter result indicates that the glomus cells are innervated not only by the centripetal fibres, but also—via the glossopharyngeal nerve—by centrifugal fibres having their trophic centre in the brain stem.

The nerves to the carotid glomus which predominantly traversed the capsule at the upper pole of the glomus (White 1935/36) formed a coarse-meshed plexus. From this plexus there formed an interlobular, a perilobular, and an intra-lobular plexus (Vaida, Duca & Lazăr 1966). When entering the lobules most of the nerves were lined only with Schwann's sheaths (Ross 1959). Whether the nerves in the lobules formed synapses with the glomus cells, as believed by de Castro (1926, 1928, 1940, 1951) or whether they formed a syncytium with the cells (Martínez 1939, Meijling 1937) was previously a controversial point, but electron microscopy has now solved the problem in favour of de Castro's view (cf. section 3.3).

3.1.8. Development

As to the source from which the carotid glomus develops, the reports have differed widely: (1) From the mesoderm, (2) from neuroectodermal cells in the cranial nerves, (3) from the epibranchial ectoderm, (4) from the sympathetic trunk, and (5) from the pharyngeal entoderm. As already established in section

1.2, the carotid glomus is not of entodermal derivation (cf. section 1.2.3), and the sympathetic cells are secondary phenomena and small in number (cf. section 1.2.5). Recent studies giving the results mentioned under (1)–(3) will be reviewed in some detail.

Re (1). Investigations showing that the carotid glomus is derived exclusively or predominantly from the mesoderm around the internal carotid artery: Rabl (1922)—whose paper gives a thorough review of the earliest embryological studies—found that the carotid glomus in guinea pigs developed from the local mesoderm. Smith (1924) obtained a similar result by studying rats, calves, cats, pigs, and human specimens. To the primary mesodermal primordium there migrated, depending upon the nature of the experimental animal, varying quantities of cells from the sympathetic trunk, vagus nerve, and glossopharyngeal nerve. Similar findings were made by Hammar (1934) in man and by Celestino da Costa (1935) in bats and rabbits. The most thorough and most quoted study supporting the mesodermal theory is Boyd's (1937a) of more than 125 human embryos and fetuses. His results have later been confirmed in a similar material by Murillo-Ferrol (1961). In embryos of a crown-rump length 12.5 mm Boyd found a primary condensation of mesodermal cells lying like a cuff around the commencement of the third aortic arch. This arterial segment corresponds to that part of the internal carotid artery where the carotid sinus develops. The cells in this condensation were large, polygonal, and pale. At this stage the sinus nerve was in contact with the glomus primordium. Along the nerve small cells with dark nuclei were migrating. Later, at the 26–36 mm stage, similar cells migrated to the primordium along the sinus nerve and along the branches of the vagus nerve and sympathetic trunk which had developed in the meantime. In Boyd's opinion the large pale mesodermal cells developed into the essential cells in the carotid glomus, the small dark cells being pre-neuroblasts which largely underwent retrogression. In a study of rabbits d'Agostini (1959) was unable to establish whether the specific cells in the carotid glomus developed from the mesenchymal proliferation or from the cells which reached the primordium by way of the nerves from the glossopharyngeal nerve and superior cervical ganglion.

Re (2). Investigations showing that the carotid glomus was derived exclusively or predominantly from neuroectodermal cells in the sensory ganglia of the glossopharyngeal and vagal nerves: According to Benoit (1928) there was in mice a cellular expansion from the ganglia of the vagus nerve along the internal carotid to the bifurcation, where the cells formed a perivascular cuff on the commencement of the artery. In mammals Watzka (1938) found the parenchymal cells in the carotid glomus to have developed from cells derived from the vagus as well as from the glossopharyngeal nerve. In pigs de Winiwarter (1939) demonstrated that the neuroectodermal cells were derived essentially from the glossopharyngeal ganglia and possibly from ectodermal cells which took part in the formation of these ganglia. In studies on rabbits Ito (1950)

supported the hypothesis that the carotid glomus had developed from cells in the glossopharyngeal nerve.

Re (3). Investigations showing that the carotid glomus was exclusively or predominantly of ectodermal derivation, from an epibranchial thickening in the ectoderm at the site of the 2nd, 3rd, or 4th branchial groove: In ducks Szepsenwol (1935) found the carotid glomus to have developed from ectodermal cells from the placode in the 4th branchial groove, whereas Argaud (1941) believed that the placode which supplied the carotid glomus with cells was in the 3rd branchial groove. In a comprehensive study on sheep Batten (1960) demonstrated that ectodermal cells to the carotid glomus were derived from a placode in the 2nd branchial groove. The cells in this ectodermal thickening migrated partly to the primordium of the inferior glossopharyngeal ganglion and partly, in several waves, direct from the placode to the sinus nerve and further along the nerve to a mesodermal condensation which made up the primary primordium of the carotid glomus. Rogers (1965), studying rats, could not establish whence the cells in the primary primordium around the commencement of the third aortic arch were derived, but could not rule out that they might be ectodermal. To the primary primordium there was a migration in several waves of small, dark cells along the sinus nerve. In a material of chicks (Murillo-Ferrol 1967) the first visible primordium of the carotid glomus was a small condensation whose cells were from the epibranchial microplacodes in the 2nd and 3rd branchial groove.

The controversial views concerning the histogenesis of the carotid glomus are apparant from this brief outline. However, it must be borne in mind that a very large part of the reviewed investigations were carried out before it was realized that the adult carotid glomus is built up of several cell types. Assuming that these cell types have been derived from different sources, the following hypothesis can unite the conflicting results:

The chief cells in the carotid glomus have developed from an epibranchial placode. The ectodermal cells from the placode take part in the formation of the glossopharyngeal ganglion whence they migrate, by way of the sinus nerve, to the glomus primordium, possibly direct from the placode to the sinus nerve. In support of this assumption it may be adduced that all authors, except Batten (1960), agree that the first primordium and the sinus nerve appear at very much the same time. The circumscribed thickening of the wall in the commencement of the internal carotid artery, which Boyd (1937a) and Murillo-Ferrol (1961) in studies of human embryos considered the primary anlage of the carotid glomus, possibly represents a stage in the development of the carotid sinus. At least this applies in dogs. Studying this animal Nielsen (1968) found at the site of the future carotid sinus a very thick cellular tunica media which did not diminish until around birth, when the carotid sinus attained its characteristic architecture with a thin wall composed of an elastic media and a relatively thick tunica externa. Schwarz-Karsten (1944) believed that the thickened vessel

wall in pig embryos existed prior to the actual nervous primordium of the carotid glomus and that it was due to the blood vessels found later in the glomus primordium.

The supporting cells—which in their relation to the nerve fibres and chief cells are very reminiscent of Schwann cells and other perineuronal cells in the central nervous system and peripheral ganglia—are neuroectodermal, migrating along all the nerves leading to the carotid glomus, primarily the glossopharyngeal. Rogers (1965) has suggested that the supporting cells have developed from the small, dark cells.

Vessels, stroma, and pericytes are mesodermal and have developed in the local mesenchyme around the commencement of the internal carotid artery. That this mesenchymal component of the carotid glomus primordium is secondary has been claimed by Ito (1950), Watzka (1938), and de Winiwarter (1939).

Ganglion cells and any chromaffin cells that may be present are of sympathetic origin.

3.2. Present Investigations

3.2.1. Light Microscopy

The carotid glomus, from the right as well as the left side, was studied in preparations like the one shown in Fig. 3.1. The right carotid glomus from foetus cr 61 was not examined in the electron microscope. In the light microscope the carotid glomus (Fig. 3.2) presented itself as an oval cellular condensation in the mesenchyme between the internal and external carotid arteries. The mean of the maximum transverse and craniocaudal diameters was approx. $250 \times 390 \mu\text{m}$. Its cells formed strands and whorls around the vascular lumina. No connective-tissue capsule had formed, but the surrounding fibroblasts were oriented concentrically with the surface. At its upper pole the organ was delimited from the surrounding immature connective tissue by a plexus of thin-walled vessels. In between the cell groups there were connective-tissue spaces communicating with the surrounding mesenchyme.

In the glomus parenchyma it was possible to distinguish, though with some difficulty, two types of cell, chief cells and supporting cells (Figs. 3.3, 3.4, 3.5, 3.6). The chief cells, which appeared in the light microscope to be about eight times more common than the supporting cells, were characterized by their circular or oval nuclei measuring about $7 \mu\text{m}$. The nucleoplasm was pale, the chromatin particles delicate, evenly distributed, and faintly staining. In the periphery of the nuclei and in small central areas dense chromatin fragments were observed. There were nucleoli of an eccentric situation, in contact with the peripheral chromatin condensation. The cytoplasm was ample, pale, with scattered, deeply stained small granules and a few larger, apparently empty vacuoles.

At a high magnification these cytoplasmic structures lent the cells a cloudy appearance. In areas where the cells were densely arranged, the cell borders were difficult to discern. The supporting cells were characterized by their nuclei, which were smaller than those of the chief cells and more irregular in shape, as a rule oblong or semilunar, clinging around the chief cells. The nuclear structure was darker than in the chief cells, the chromatin being assembled in coarser fragments. The cytoplasm around the nucleus was scanty. In a few cases cytoplasmic extensions, slung around the chief cells, could just be traced.

The vessels, dilated because of the distention from the infusion fixation with glutaraldehyde, were thin-walled and presented themselves in sections either as narrow, regular or as larger, irregular lumina. As the vessel wall in both types was of the same structure, it was not possible to tell whether the smaller vessels were merely specially sectioned areas of the larger ones. The vessel wall was made up of two layers of cells, a continuous layer of endothelial cells and a discontinuous layer of pericytes. The pericytes had relatively dark nuclei with a coarse chromatin pattern, and were discernible from supporting cells and endothelial cells only by virtue of their perivascular situation.

Nerve fibres could not be identified in the parenchyma. The sinus nerve and smaller branches in the periglomerular mesenchyme were distinctly apparent (Fig. 3.2).

3.2.2. Electron Microscopy

Electron microscopy revealed in low power view (Fig. 3.7) chief cells, supporting cells, bundles of nerve fibres, and vessels with endothelial cells and pericytes.

Fine Structure of Chief Cells.

The chief cells sectioned through the nucleus were oval or drop-shaped. In addition, there were obliquely, transversely, and longitudinally sectioned processes containing osmiophilic granules. Three-dimensionally the cells were thus rod- or spindle-shaped having one or more processes. The nuclei, like the cells, were oblong. They had notches which on section might be so deep that the nuclei were kidney-shaped. The nuclear structure exhibited no special characteristics. In the ultra-thin sections it was not, as in the thick sections, paler than the nuclear structure of the supporting cells. The nuclei of the chief cells were often of an asymmetric situation in the cell, leaving a narrow cytoplasmic rim, poor in organelles, on one side and a wider cytoplasmic rim with more ample organelles on the other side (Fig. 3.9). The chromatin presented as fairly evenly distributed granules in the nucleoplasm, but more concentrated beneath the nuclear membrane. Nucleoli (Figs. 3.7, 3.9) were seen peripherally in the nucleus, often in relation to the peripheral chromatin from which, however, they could be clearly distinguished by their very electron-opaque nucleolonema. The nuclei were surrounded by two separate membranes in which there were nuclear

pores (Fig. 3.15). On a level with the pores there were breaks in the peripheral chromatin ring which therefore appeared serrated on low magnification. The inner nuclear membrane was closely wrapped around the chromatin, whereas the outer one might be heavily folded, with vesicular processes in the cytoplasmic ground substance (Fig. 3.13). This lent the perinuclear cistern a varying width.

The cytoplasm showed varying electron opacity at low magnification. A distinction could be made between pale and dark chief cells, but transitional forms were common (Fig. 3.7). It could not be decided whether the difference in electron transparency was a property inherent in the cytoplasmic ground substance or caused by a greater accumulation of organelles in the dark than in the pale cells.

The plasma membrane, which was trilaminar, exhibited only a few special features. Occasionally there would be invaginations, indicating micropinocytotic activity (Fig. 3.18). In limited areas, where two chief cells were in contact, the adjacent plasma membranes were difficult to distinguish from submembranous, electron opaque material (Figs. 3.15, 3.18, 3.20). The intercellular space between the chief cells as well as between chief cells and supporting cells was about 30 nm. The plasmalemma was of a parallel course, in soft undulations. Cilia, deeply invaginated in the cytoplasm, were so rare that the pattern of the axial filament complex could not be mapped (Fig. 3.17).

Granular endoplasmic reticulum occupied only a small part of the cell volume (Figs. 3.9, 3.13). The cisterns were usually of a peripheral situation in the cells, parallel to the plasma membrane. There were rarely more than five cisterns in each stack. Solitary, shorter cisterns and small ribosome-lined vesicles were present throughout the cytoplasm, and so were free ribosomes, which were estimated to occur—in the form of polyribosomes or of solitary granules—in the same numbers as the membrane-bound ribosomes (Fig. 3.16). In the cytoplasm there occurred also agranular vacuoles which were difficult to classify (Fig. 3.13). A number of these vacuoles presumably belonged to the agranular endoplasmic reticulum or the Golgi complex. It could not be ruled out that the pale vacuoles might have been caused by insufficient fixation entailing distention of the membrane system belonging to the specific granules, the Golgi zones, the endoplasmic reticulum, or mitochondria. The vacuole membranes might be heavily folded and discontinuous, but the latter might possibly be a consequence of tangential sectioning. Occasionally there were swollen, disintegrated mitochondria and pale, non-membrane-bound areas in the cytoplasm as well as the blebbing phenomenon. These suspicious phenomena were not restricted to the chief cells.

The Golgi complex (Figs. 3.9, 3.13), which was close to the centrosome, was a constant finding. The complex was made up of stacks of cisterns, vacuoles, and vesicles. The membrane of the latter was occasionally coated on the external aspect. In several zones there was, at the terminal distended ends of the cisterns,

an accumulation of a homogeneous, very electron-opaque material (Fig. 3.21). There was no accumulation of specific granules in relation to the Golgi zone, but adjacent specific granules were of a shape divergent from that of the typical granule. Mitochondria (Figs. 3.13, 3.16) were oval, rod-or cigar-shaped, rarely branched. Their transverse diameter was around 300 nm. Mitochondrial cristae were densely arranged, straight, and parallel and often went right across the mitochondrion. The matrix was of dense structure and contained a few mitochondrial granules. Microtubules of indeterminate length and a diameter just over 20 nm were lying as single, scattered, crossed tubules in the perinuclear cytoplasm (Fig. 3.13), but occurred in the chief cell processes in dense, parallel bundles (Fig. 3.14). Lysosome-like, membrane-bound bodies of a size like mitochondria were fairly common. A number of bodies contained detritus-like, laminated substance (Fig. 3.15) or small vesicles (Fig. 3.16), whereas the content of others was homogeneous (Fig. 3.13). In the latter it was not always possible to distinguish a limiting membrane, so that it might be endogenous lipid. Glycogen was possibly present in a few cells. The particles were only slightly larger than the ribosomes, and although with the lead stain used they ought to be more opaque than ribosomes, alpha-glycogen particles and polyribosomes were apt to be confused. The same applied to beta-glycogen particles and solitary ribosomes.

The specific granules were the most characteristic fine structure in the chief cells. They were present in extremely varying numbers in the individual cells, from less than 10 to more than 100 in each section that hit the nucleus of a chief cell. Granules were not more numerous in the dark than in the pale chief cells. They were observed throughout the cytoplasm, juxta-nuclear as well as in the processes, but were otherwise of a very unequal distribution. There was no accumulation of granules in relation to the organelles of the chief cells, neither at the Golgi zones, at the granular endoplasmic reticulum, at the plasma membrane, or at the plasma membrane where it was in contact with nerve fibres.

A typical granule (Fig. 3.22) consisted of a central very electron-opaque, homogeneous nucleus surrounded by a trilaminar membrane of a thickness like the outer mitochondrial membrane. Between the dark nucleus and the membrane there was a pale space, about 10 nm wide. The contents of this space were a little more electron-opaque and rather more heavily structured than the cytoplasmic ground substance. In ultra-thin sections the granules were found to be of varying size, due undoubtedly in part to a large proportion of the granules in a given section representing tangentially sectioned parts of whole granules, the thickness of the sections being about half that of the granule diameter (Fig. 3.14). Most granules were approximately circular on section, their three-dimensional shape therefore spherical or approximately spherical. A number of granules differed from the typical shape. In places the vesicular membrane could not be distinguished, because it was lying tight around the electron-opaque nucleus or because it was tangentially sectioned. The vesicle might be too large

in relation to its nucleus. In that case the nucleus was asymmetric, in contact with one side of the vesicle. The wider the space the paler its contents. This might suggest an artefact-conditioned dilatation of the vesicle. The contents of the space between a dilated vesicle and its nucleus were more heavily structured than the contents of the typical granule and held very delicate granules or radial streaks from the nucleus. In a few vesicles there were apparently two separate nuclei, but this phenomenon might be due to oblique sectioning of the membranes around two closely placed granules.

Calculated as the mean of 1688 measurements of the vesicles in 1246 specific granules from the seven electron-microscoped carotid glomera, the granular diameter was 110 nm, standard deviation 18, 95 % interval 75–146. For data concerning each individual glomus, please consult Table II.

Fine Structure of the Supporting Cells.

Among cells sectioned through the nucleus supporting cells were 2–3 times less common than chief cells. In ultra-thin sections the chromatin structure in the nuclei of the supporting cells was not denser than in the chief cells. The shape of the nuclei was very irregular and varying, often characterized by nerve fibres or chief cells lying in the vicinity (Figs. 3.7, 3.8, 3.9). The nuclei contained nucleoli. The shape of the supporting cells was difficult to analyse, the cells being provided with narrow extensions making their way far in between the glomus cells, especially around the chief cells. The perinuclear cytoplasm was scanty, with few organelles. The most predominant structures were small uncharacteristic mitochondria, short, flat granular cisterns, free ribosomes, and pale vacuoles. Golgi zones, cilia, lysosomes, and centrioles were occasionally observed.

Nerve Fibres.

Nerve fibres were observed in large numbers between the cells. They were of varying diameter, presumably due in part to their having been sectioned at a different distance from their endings (Figs. 3.7, 3.8, 3.19, 3.20). The fibres had a pale axoplasm which contained longitudinal, about 20 nm thick neurotubules, a few small, round mitochondria, and small vesicles which occasionally contained an electron-opaque nucleus. There were no myelinated nerve fibres.

Relationship Between Chief Cells, Supporting Cells, and Nerve Fibres

Supporting cells and their extensions surrounded one or more chief cells (Figs. 3.7, 3.9, 3.10), but the encapsulation of the chief cells was not complete. In large areas the chief cells were mutually in contact, and in smaller areas the chief-cell plasma membranes were in direct contact with wider intercellular interstices (Figs. 3.12, 3.14). The relation of the chief cells to the supporting cells could be most aptly described as mesaxonic; the chief cells – like the nerve fibres in Schwann cells—were embedded in the supporting cells. The

nerve fibres in the carotid glomus were either between chief cells, between chief cells and supporting cells, or were embedded through mesaxons in the latter (Figs. 3.7, 3.8, 3.19, 3.20). After reviewing numerous electron microscopic photomicrographs I got the impression that frequently chief cells and nerve fibres were embedded in supporting cells through the same mesaxons (Fig. 3.8). Where chief cells or supporting cells were in contact with nerve fibres (Figs. 3.19, 3.20) there were, neither in the nerve fibres nor in the cells, any signs of synaptic specializations. There was no accumulation of synaptic vesicles, of specific granules or mitochondria, no button-shaped nerve endings, and no thickenings of the plasma membrane at the sites of contact.

Vessels and Connective Tissue.

The vascular endothelium exhibited no characteristic appearances apart from a few fenestrations (Figs. 3.11, 3.12). Considerable areas of the outside of the endothelial cells were covered with pericytes and their processes (Figs. 3.7, 3.10). The chief cells were rarely in direct contact with the endothelial cells. The two cell types were separated, either by pericytes or by supporting-cell processes, or by both. In the carotid glomus there were a few fibroblasts, predominated by a well-developed system of long, straight, rather wide cisterns studded with ribosomes. In the intercellular substance between groups of parenchymal cells and between these groups and the vessels there were fibroblasts and scattered bundles of collagen fibres. From the fine structure it was not possible to distinguish supporting cells from Schwann cells, but I found cells whose mesaxons contained nerve fibres, but no chief cell processes.

3.3. Discussion

My observations of the light microscopic structure of the carotid glomus are in conformity with the findings of Murillo-Ferrol (1961) and Boyd (1937a) in foetuses of the same size. The small dark cells, which Boyd interpreted as preneuroblasts, and which underwent retrogression during their continued development, proved to be supporting cells in my electron microscopic investigations. In adult individuals about 15 % of the cells may be identified as supporting cells in the light microscope (de Kock 1954), and 25–50 % in the electron microscope (Grimley & Glenner 1967). These statements correspond to my findings in the foetus: In the light microscope the ratio supporting cell: chief cell was 1:8, in the electron microscope 1:3. Thus, since the relationship between the number of the two cell types is of the same order in adults and foetuses, it must be assumed that Boyd's preneuroblasts do not undergo retrogression and that Boyd confused the two types of cell in the light microscope.

The size of the specific granules in the chief cells from human materials has been stated to be 80–230 nm (Kraus & Martínek 1968), 70–100 nm (Feria-

Velasco, González-Angulo & Zavala 1966), 98 nm (minimum and maximum diameter 30 and 240 nm) (Simárszky & Lapis 1970), 130 nm (Grimley & Glenner 1967, 1968), 100–200 nm (Böck, Stockinger & Vyslonzil 1970), and in chief cells from foetuses 150–200 nm (Battaglia 1969). The stated size of granules from animals shows a corresponding variation: 50–150 nm (Lever & Boyd 1957, Lever, Lewis & Boyd 1959), 60–80 nm (Ross 1959), 80–90 nm (Kobayashi & Uehara 1970), ca. 100 nm (Palkama 1965), 60–160 nm (de Kock & Dunn 1966), 35–190 nm (Biscoe & Stehbins 1966), 40–230 nm (Al-Lami & Murray 1968a), and 50–150 nm (Hess 1968). Considering that the fixation exerts a marked influence upon granular size and appearance (Duncan & Yates 1967) and that the inaccuracy of the measurement is appreciable, these statements must be said to be in keeping with my measurements which showed a mean of 110, minimum value 58 nm and maximum value 188 nm.

In addition to the specific granules practically all authors have mentioned or described mitochondria, endoplasmic reticulum, and Golgi complex in the chief cells. In the Golgi zone signs of granulogenesis have been found (Kraus & Martínek 1968). Pale and dark chief cells have been thoroughly described (de Castro & Rubio 1968, Fería-Velasco, González-Angulo & Zavala 1966, Grimley & Glenner 1967, 1968, Höglund 1967, Kraus & Martínek 1967, Lever, Lewis & Boyd 1959, Simárszky & Lapis 1970). According to Grimley & Glenner the dark cells made up 5–20 % of the total number of chief cells. Most authors incline to the view that the difference is due to the cells at the time of fixation being in different functional stages, but it has not yet been elucidated whether there is a question of qualitative changes in the hyaloplasm and/or quantitative changes in the organelle content. In addition, lysosomes of extremely varying appearance have been observed (Al-Lami & Murray 1968a, Battaglia 1968, Böck, Stockinger & Vyslonzil 1970, Grimley & Glenner 1968, Kraus & Martínek 1968, Ross 1959, Simárszky & Lapis 1970), large vacuoles with pale contents (de Castro & Rubio 1968, de Kock & Dunn 1966), coated vesicles (Biscoe & Stehbins 1966, Höglund 1967), microtubules (Biscoe & Stehbins 1966, Grimley & Glenner 1968, Hess 1968) having a diameter of 25 nm (Böck, Stockinger & Vyslonzil 1970), lipids (Al-Lami & Murray 1968a, Böck, Stockinger & Vyslonzil 1970, Fería-Velasco, González-Angulo & Zavala 1966, Grimley & Glenner 1967, 1968, Hess 1968), scanty glycogen (Böck, Stockinger & Vyslonzil 1970), and desmosomes between the chief (Al-Lami & Murray 1968b, Biscoe & Stehbins 1966, Böck, Stockinger & Vyslonzil 1970, Grimley & Glenner 1968). Cilia have been found in the chief cells (Battaglia 1968, Böck, Stockinger & Vyslonzil 1970, Hess 1968, Kraus & Martínek 1967). The fibril pattern was $9 + 0$ in cats and rabbits (Biscoe & Stehbins 1966), $9 + 2$ in man (Abrahám 1969). The similarity of the supporting cells and Schwann cells has been pointed out by int. al. Böck (1970c), Böck, Stockinger & Vyslonzil (1970), Grimley & Glenner (1967, 1968), Hess (1968), Lever, Lewis & Boyd (1959), and Ross (1959).

Thus, in my foetal material the glomus cells showed all the fine structural features that have been described previously.

The relationship between chief and supporting cells has been described in detail by de Kock & Dunn (1966) who used serial ultra-sectioning. According to their findings the plasma membrane of the chief cells, wherever it was not in contact with other chief cells or nerve fibres, was lined with supporting-cell sheaths. According to Biscoe & Stehbens (1966) and Duncan & Yates (1967) there is a basal lamina around groups of chief and supporting cells.

The vascular endothelium is fenestrated (Al-Lami & Murray 1968a, 1968b, Biscoe & Stehbens 1965, 1966, Grimley & Glenner 1967, 1968, Simásky & Lapis 1970), surrounded by pericytes (Fería-Velasco, González-Angulo & Zavale 1966, Grimley & Glenner 1967, de Kock & Dunn 1966, Simásky & Lapis 1970), and lined with a basal lamina (Fería-Velasco, González-Angulo & Zavale 1966, Grimley & Glenner 1968, de Kock & Dunn 1966, Lever, Lewis & Boyd 1959, Simásky & Lapis 1970).

A number of nerve fibres, especially in the peripheral areas of the lobules, are myelinated (Al-Lami & Murray 1968a, Fería-Velasco & González-Angulo 1968, Grimley & Glenner 1967, Ross 1959). The nerve fibres contain neurotubules, fibrils, and occasionally 40–60 nm large vesicles with an electron-opaque nucleus (Ábrahám 1969, Grimley & Glenner 1968, Simásky & Lapis 1970). Several types of nerve terminals have been encountered in the carotid glomus: (1) Specialized synaptic contact between the nerve endings and the chief cells. The nerve endings are button-shaped and embedded in invaginations in the plasmalemma of the chief cells. The synaptoplemma is bound together by desmosomes, and small mitochondria have accumulated in the axoplasm. Morphologically a distinction has been made between efferent synapses (Ábrahám 1969, Al-Lami & Murray 1968a, Battaglia 1968, Biscoe & Stehbens 1965, 1966, Böck 1970c, de Castro & Rubio 1968, Grimley & Glenner 1967, Hess 1968, Höglund 1967, de Kock & Dunn 1966, 1968, Kraus & Martínek 1970), characterized among other things by an accumulation of synaptic vesicles on the axonal side of the synaptoplemma, and afferent synapses (Ábrahám 1969, Al-Lami & Murray 1968b, Kobayashi & Uehara 1970) characterized among other things by accumulation of synaptic vesicles on the cytoplasmic side of the synaptoplemma. The synaptic vesicles were about 50 nm large and occasionally contained an electron-opaque nucleus. (2) "En passant" or "basket" contact. The nerve fibres are lying, over long distances, in contact with the plasma membrane of the chief cells and have a relatively empty axoplasm (Al-Lami & Murray 1968a, Böck 1970c, de Castro & Rubio 1968, Grimley & Glenner 1968, Höglund 1967, de Kock & Dunn 1964, Ross 1959). (3) Possibly, a number of the nerve fibres end in the mesaxons of the supporting cells without attaining contact with the chief cells (de Kock & Dunn 1964, 1966, 1968, Ross 1959). (4) Mitochondrial sacks, i. e. about 10 μ m terminal vesiculations of nerve fibres, filled with mitochondria and a few 40–60 nm large non-

granular and 80–120 nm large granular vesicles. The mitochondrial sacks are surrounded by supporting cells. They rarely attain contact with the chief cells, and if so in the form of a non-specialized connection (Böck 1970c, Böck, Stockinger & Vyslonzil 1970).

A problem which still remains unelucidated is whether the chief cells contain several types of specific granules. After glutaraldehyde-osmium fixation of the carotid glomus of cats Morita, Chiocchio & Tramezzani (1969) distinguished between four types of chief cells (I–IV). These types were characterized especially by their granular size and structure, considered to depend upon which biogenic amine the cell contained (dopamine in type II, 5-hydroxytryptamine in type III, noradrenaline in type I, and adrenaline in type IV). Fería-Velasco, González-Angulo & Zavala (1966) reported that the granules in the dark chief cells were somewhat larger than those in the pale ones. According to Kraus & Martínek (1968) there were, within the same cell, primary small granules and secondary, somewhat larger granules. Böck, Stockinger & Vyslonzil (1970) found numerous 100–200 nm large granules and fewer 250–500 nm large granules within the same cell. Kobayashi & Uehara (1970) found—apart from the disseminated 80–90 nm large type of granule predominating the cytoplasm—30–40 nm large electron opaque granules surrounded by a membrane close to the nerve endings.

Thus, there is a divergence between the reported studies and mine with respect to the supporting-cell cover of the chief cells, the differentiation of granules in the chief cells, the occurrence of synaptic specialization, myelination of the nerve fibres, and the occurrence of basal laminae around vessels and glomus cells. The explanation of these divergences may be that my material consists of not fully developed individuals. Within the brief developmental course represented by the four fetuses there were no morphological changes in the organ that could be ascribed to a variation in the degree of development.

Aorticopulmonary Glomera

4.1. Review of the Literature

4.1.1. *Synonyms for Aorticopulmonary Glomera*

Synonyms covering the subclavian glomus as well as the aorticopulmonary glomera.

Paraganglion caroticum inferius (Latin: Rabl 1922).

Glomus aorticum (Latin: Addison & Comroe 1938).

Aortic arch bodies (English: Hammond 1941).

Aortic bodies (English: Comroe 1939, Gernandt 1946, Heymans & Neil 1958, Howe 1956).

Cardio-aortic bodies (English: Hollinshead 1940a).

Aortico-pulmonary glomus tissue (English: Verity, Hughes & Bevan 1964).

Thoracic aortic glomera (English: Elliott 1965a).

Synonyms for the inferior, middle, and superior aorticopulmonary glomera

Paraganglion aorticum (Latin: Penitschka 1930), aortic paraganglion (English: Nonidez 1936).

Paraganglion aorticum supracardiale (Latin: Penitschka 1931).

Paraganglion supracardiale (Latin: Palme 1934), paraganglion supracardiale (French: Goormaghtigh & Pannier 1939).

Glomus pulmonalis (Latin: Nonidez 1936).

Paraganglion épocardique (French: Goormaghtigh & Pannier 1936).

Pulmonary-arch bodies (English: Boyd 1937a).

Supracardial bodies (English: Hollinshead 1940a).

Aortic body group 4 (English: Howe 1956).

Paraganglio aortico-polmonare (Italian: Muratori 1960).

Aortico-pulmonary bodies (English: Boyd 1961).

Synonyms for the superior aorticopulmonary glomus

Paraganglion supracardiale superius (Latin: Palme 1934).

Oberes Herzparaganglion (German: Seto 1935).

Paraganglio aortico superiore (Italian: Muratori 1936).

Paraganglio cardioaortico superiore (Italian: Muratori 1937).

Paragânglio cádio-aórtico superior (Spanish: Strecht Ribeiro 1945).

Paraganglion supracardiale cranialis (Latin: Kohfahl 1952).

Paraganglio aortico-polmonare superiore (Italian: Muratori 1960).
 Paraganglio aortico-polmonare botallico (Italian: Muratori 1960).
 Superior aortico-pulmonary glomus (English: Boyd 1961).
 Superior supracardiac paraganglia (English: Kovrizhko 1963).
 Glomera aortica (Latin: Becker 1966a).

Synonyms for the middle aorticopulmonary glomus

Mittleres Paraganglion (German: Palme 1934, p. 400).
 Paraganglio aortico-polmonare medio (Italian: Muratori 1960).
 Middle aortico-pulmonary glomus (English: Boyd 1961).
 Glomus pulmonale (Latin: Heyers 1963, Knoche & Schmitt 1963, Krahel 1962).

Synonyms for the inferior aorticopulmonary glomus

Paraganglion supracardiale inferius (Latin: Palme 1934).
 Unteres Herzparaganglion (German: Seto 1935).
 Paraganglio aortico inferiore (Italian: Muratori 1936).
 Paraganglio cardioaortico inferiore (Italian: Muratori 1937).
 Paragânglio cárdio-aórtico inferior (Spanish: Ribeiro 1945).
 Paraganglio polmonare (Italian: Muratori 1937).
 Paraganglion supracardiale caudalis (Latin: Kohfahl 1952).
 Paraganglio aortico-polmonare inferiore (Italian: Muratori 1960).
 Inferior aortico-pulmonary glomus (English: Boyd 1961).
 Inferior supracardiac paraganglia (English: Kovrizhko 1963).

Synonym covering the inferior as well as middle aorticopulmonary glomera.
 Glomera coronaria (Latin: Becker 1966a).

This survey should be taken with a grain of salt. The assignation of the glomera to the three groups is *per se* difficult and must always be based upon an estimate. For instance, it is possible that the aggregations which Penitschka (1931) described as paraganglion aorticum supracardiale did not represent all aorticopulmonary glomera, but merely the superior aorticopulmonary glomus. The nomenclature is confused: The term glomus or paraganglion pulmonale may be used by different authors to designate either all the glomera, just the middle aorticopulmonary glomus, or just the inferior aorticopulmonary glomus. The distinction from the adjacent glomera gives rise to problems. Several workers, int. al. Boyd (1961) have claimed that the "chromaffin" tissue that was described just after the turn of the century on the cardiac base represented the inferior aorticopulmonary glomus, whereas I assign it to a separate group (cf. section 8.4). The distinction upwards, from the left subclavian glomus, is also vague. For instance, it is a matter of discussion whether Howe's (1956) aortic body group 3 should be assigned to the superior aorticopulmonary glomus or to the left subclavian glomus (cf. section 5.3). In the present paper it is assigned to the latter.

4.1.2. Site

In the interstice between the aorta and pulmonary trunk in a human material Busachhi (1912/13) found clusters of cells extending from the ductus arteriosus to the semilunar valves. He considered that they belonged to the chromaffin system. Twenty years later, when Penitscka (1930, 1931) recognized the similarity of the tissue to the carotid glomus, investigations into these structures gathered speed. In a human material of eight fetuses of the size 12–41 cm crown-heel length, two newborn infants, two 8-year-old children, one 22-year-old woman, and one 25-year-old man Palme (1934) distinguished between an upper, a middle, and a lower group of glomus tissue below the aorta. The upper group, consisting most often of a small ventral and a larger dorsal collection, was situated below the aortic arch in relation to the ductus arteriosus. The middle group, which was the smallest one, being about 200 μm in diameter, was situated below the bifurcation of the pulmonary trunk. The lower group, between the pulmonary trunk and the ascending aorta, was just cranial to the origin of the left coronary artery. In several subsequent studies a distinction was made in man between merely two groups corresponding to Palme's upper and lower group (Kovrizhko 1963, Muratori 1936, 1937, Seto 1935, Strecht Ribeiro 1945). In conformity, Boyd (1937a), in human embryos and fetuses, found an upper collection in the angle between the ductus arteriosus and descending aorta and a lower one situated on the right of and on the upper surface of the pulmonary trunk, occupying a varying part of the area between the left coronary artery and the bifurcation of the pulmonary trunk. The lower group Boyd (1961) later divided into two, corresponding to Palme's middle and lower group.

In a material of 28 older human fetuses and newborns Becker (1966a, 1966b) found 3–5 glomera in the connective tissue between the aorta and pulmonary trunk immediately cranial to the root of the left coronary artery (Becker's group 2), 2 smaller glomera on a level with the bifurcation of the pulmonary trunk between the aorta and the right pulmonary artery (Becker's group 3), and a group of about 6 glomera between the bifurcation of the pulmonary trunk and the arch of the aorta (Becker's group 4). Becker's material of adults permitted verification only of the inferior and middle aorticopulmonary glomus (Becker 1966a).

The middle aorticopulmonary glomus has been the subject of independent investigation (Cecio, Vacca & Vacca 1962, Edwards & Heath 1969, Heyers 1963, Knoche & Schmitt 1963, Krah1 1962). These authors found the organ to be embedded in the adventitia of the pulmonary trunk in or immediately below its bifurcation. Krah1 (1962) thought that glomus tissue had not previously been described dorsal to the pulmonary trunk. This is not correct, since Nonidez, as early as 1937 in a study of dogs—which were also used in Krah1's material—found not only an upper and a lower group, but also a fairly large group in

the bifurcation of the pulmonary trunk and adjacent to it several smaller clusters more caudally in the adventitia of the posterior wall of the pulmonary trunk.

In dogs (Coleridge, Coleridge & Howe 1970, Nonidez 1937) and in cats (Coleridge, Coleridge & Howe 1967, Goormaghtigh & Pannier 1939, Hollinshead 1940b, Howe 1956, Hughes 1965a, Muratori 1962a, Nonidez 1936, Palme 1934, Verity, Hughes & Bevan 1964) the glomus tissue was lying, in major or minor clusters, in chains extending on the anterior and posterior aspect of the pulmonary trunk from the base of the heart to the ligamentum arteriosum.

In other animal species it is also not possible in most cases to make a clear distinction between glomera whose site corresponds to the three groups in man. The aorticopulmonary glomera have been reported in rabbits (Becker 1966a, 1966b, Knoche & Schmitt 1963, Muratori 1937, 1962a, Penitschka 1931), rats (Krahl 1962, Palme 1934), guinea pigs (Muratori 1937), pigs (Ábrahám 1958, Schwarz-Karsten 1944), oxen (Kohfahl 1952, Krahl 1962), horses (Kohfahl 1952), monkeys (Krahl 1962), muskrats (Muratori 1959), a seal (Blessing & Hartschen 1969), and in various species of birds (Muratori 1962b, Tchong & Fu 1962, Wirtz 1968).

4.1.3. Light Microscopic Structure

The largest glomera in Becker's (1966a) human material were $750 \times 500 \mu\text{m}$ in the inferior, $250 \times 150 \mu\text{m}$ in the middle, and about $700 \times 500 \mu\text{m}$ in the superior group, in the craniocaudal direction and in cross section respectively. In foetuses and newborns the glomera were compact and lobulated. The interlobular connective tissue communicated with the surrounding connective tissue. The interlobular septa housed nerves and blood vessels. In the lobules the glomus cells were arranged in small clusters whose central regions were made up of polygonal or round cells with a delicately granular cytoplasm and somewhat eccentric, spherical nuclei of a characteristic chromatin pattern. Peripherally in the clusters, against the intralobular capillary coils, there was another type of cell which was oblong and whose nucleus had a dense chromatin pattern.

Barnard (1946) found the superior aorticopulmonary glomus to be $800 \times 600 \mu\text{m}$. It was made up of small, amply vascularized lobules whose cells were large, irregular, polygonal with ample vacuolized cytoplasm with round or oval nuclei. The groups of cells were surrounded by spindle-shaped cells.

Heyers (1963) reported that the middle aorticopulmonary glomus in children and adults was 1–3 mm in diameter. In its connective-tissue capsule there was a plexus of myelinated and non-myelinated nerves running through the interlobular connective tissue to lobules where they formed synapses with the epithelioid cells. The parenchyma contained partly large cells with granular cytoplasm and a nucleus poor in chromatin and partly smaller cells with a chromatin-dense nucleus (Edwards & Heath 1969, Heyers 1963, Knoche & Schmitt 1963).

Boyd (1961) stated that the inferior aorticopulmonary glomus was built up

of small lobules of epithelioid cells arranged around a system of blood vessels. Pericytes surrounded the endothelium. The cells and vessels had a rich innervation.

In glomera from cats too (Goormaghtigh & Pannier 1939, Nonidez 1937) a distinction has been made between large, spherical cells with granular cytoplasm and small irregular cells which Goormaghtigh & Pannier called capsule cells. Among aorticopulmonary glomera of cats Hollinshead (1940b) distinguished between two histological types. One was characterized by epithelioid cells, the other one by tortuous vessels whose walls contained relatively few epithelioid cells, embedded in thin layers or in small islets.

In relation to the glomera animals as well as human beings exhibit small solitary ganglion cells and microganglia (Barnard 1946, Cecio, Vacca & Vacca 1962, Coleridge, Coleridge & Howe 1970, Edwards & Heath 1969, Knoche & Schmitt 1963, Kohfahl 1952, Krah1 1962, Muratori 1937, Penitschka 1931, Seto 1935). According to Palme (1934) ganglion cells were more numerous in children than in adults.

According to the quantity of connective tissue a distinction has been made between two types among the aorticopulmonary glomera: Compact glomera delimited by a capsule and having lobules separated by thin connective-tissue septa. Disseminated glomera in which the lobules were scattered over larger areas. The amount of stroma depended upon the species and upon age. In cats and monkeys (Krah1 1962) and horses (Kohfahl 1952) the glomus tissue was disseminated, in oxen compact (Kohfahl 1952, Krah1 1962), but in horses as well as in oxen the amount of connective tissue increased with age (Kohfahl 1952). In man the amount of stroma increased with advancing age (Becker 1966a, Heitner 1969, Heyers 1963, Knoche & Schmitt 1963, Krah1 1962, Palme 1934). There are marked individual variations: In an embryo of 40 mm 5 glomera were found below the aortic arch (Tschernjachiwsky 1938), in a foetus 70 separate glomera have been found (Palme 1934), and in a newborn infant about 40 glomera (Blessing 1963). In a material of 8 adults the glomera were disseminated in some and compact in others (Seto 1935).

4.1.4. Electron Microscopic Structure

Knoche & Schmitt (1963), after osmium fixation, studied the middle aorticopulmonary glomus of rabbits. They distinguished between glomus cells and supporting cells. The glomus cells were connected by desmosomes and invested by supporting cells. The chromatin structure of the glomus cells was finely granular with condensations beneath the nuclear membrane. Cells with a dark cytoplasm were more common than cells with a pale cytoplasm. The glomus cells contained endoplasmic, granular and agranular, reticulum, free ribosomes, Golgi complex, mitochondria, and a few droplets of lipid. In most glomus cells there were osmiophilic granules enveloped by a vesicle about 100 nm in diameter.

Nerve fibres were embedded through mesaxons in cells, but the authors were unable to ascertain whether these were special supporting cells or Schwann cells. Where nerve fibres and glomus cells were adjoining, the plasma membranes showed ample contrast, but there was no accumulation of organelles to indicate whether a nerve fibre or a glomus cell were to be interpreted as the post- or presynaptic element. In the pericapillary space there were fibrocytes, nerves, and collagen fibres. The endothelium and glomus cells were surrounded each by its basal lamina.

Battaglia & Mariani (1970) studied rabbit aorticopulmonary glomera fixed in 5 % glutaraldehyde. Their description is in accordance with Knoche & Schmitt's. However, the satellite cells contained filaments and tubules and the nerve endings were button-shaped, contained synaptic vesicles and were bound by desmosomes to the specific cells which contained osmiophilic granules of 50–200 nm.

4.1.5. Biogenic Amines

Although the cells in the aorticopulmonary glomera most often stained yellow or at times took no stain from chromium salts, Busacchi (1912/13) assigned them to the chromaffin system. Penitschka (1931)—recognizing the similarity of the bodies to the carotid glomus—reported that after chromium fixation the cytoplasm exhibited a finely granular pattern. A similar delicate granulation was described by Nonidez (1936), Muratori (1936), and Goormaghtigh & Pannier (1939), whereas Chumasov (1970) stated that in cats these bodies gave a distinct reaction. Concerning the chromaffinity in the inferior aorticopulmonary glomus Boyd said: "There is a suggestion of a yellowish tinge, but nothing more" (Boyd 1961, p. 129). Others have claimed that the glomera were non-chromaffin (Barnard 1946, Becker 1966a, Cecio, Vacca & Vacca 1962, Knoche & Schmitt 1963, Kohfahl 1952, Strecht Ribeiro 1945). A few genuine chromaffin cells have been found in the organs in cats (Goormaghtigh & Pannier 1939, Muratori 1962b), rabbits (Penitschka 1931), rats and pigs (Muratori 1962b), and horses (Kohfahl 1952). Studying human foetuses Palme (1934) found chromaffin cells in the superior and inferior aorticopulmonary glomera, but in adults they had completely disappeared from the superior glomus. In a large human material of a wide age range Kovrizhko (1963) found the chromium reaction in the superior glomus to be "mild", whereas the inferior glomus was distinctly chromaffin from the age of 3 years and very faintly staining with chromium salts from the age of 7 years.

Boyd (1961) and Knoche & Schmitt (1963) found the cells in the inferior and middle glomus to be argyrophil. Becker (1966a) found neither argyrophilia nor argentaffin reaction in the chief cells of the aorticopulmonary glomera. The cells in the middle aorticopulmonary glomus of the guinea pig were argyrophil (Doležel, Kovalčík & Křiška 1968). The iodaffin reaction was positive

in cats (Chumasov 1970) and pigs (Muratori 1962b), but not in rats (Muratori 1962b). Using Tramezzani's ammoniacal silver staining, Muratori, Battaglia & Modonesi (1965a) found in the aorticopulmonary glomera from newborn cats many cells giving a positive reaction, with considerable mutual variations in the strength of reaction, whereas the reaction was largely absent in the cells of these organs from newborn rabbits. By a similar method applied to the electron microscope Battaglia & Mariani (1970) observed in rabbits a positive reaction indicating the presence of 5-hydroxytryptamine, not of noradrenaline.

By formaldehyde-induced fluorescence it has been indicated that aorticopulmonary glomera int. al. from rabbits, cats, and guinea pigs, contain predominantly noradrenaline (Becker, Drukker & Meijer 1967, Doležel, Kovalčík & Křiška 1968, Muratori, Chiarini & Battaglia 1966).

4.1.6. Vascular Supply

Investigations into the vascular supply of the glomera have given different results in the same experimental animal. Some workers have found the superior aorticopulmonary glomus to be supplied by a descending vessel having its origin in the aorta or brachiocephalic trunk and the inferior as well as middle aortic glomera by an ascending vessel. Others have found all glomera, including the superior one, to be supplied by an ascending vessel which in adult animals and adult persons usually arises from the left coronary artery. According to Nonidez (1937) the superior glomus in the dog received an artery from the posterior aspect of the aortic arch and the inferior glomus a branch from the left coronary artery. In experiments using vascular injections Coleridge, Coleridge & Howe (1970) found a corresponding ascending vessel, but the descending one was found in their material to arise from the brachiocephalic trunk. In vascular injections of cats Howe (1956) also found that the descending artery did not arise directly from the aorta, but from the posterior aspect of the brachiocephalic trunk.

In contradistinction to these findings we have the results of the studies performed by Goormaghtigh & Pannier (1939) on cats and by Knoche & Schmitt (1963) as well as by Knoche (1966) on adult persons and animals, including cats and dogs. These authors considered that all aorticopulmonary glomera were supplied by one ascending vessel which usually arose from the left coronary artery, but might arise from the right coronary artery (or direct from the bulb of the aorta) or more rarely from both.

In studies of the middle aorticopulmonary glomus from a large number of experimental animals, including dogs and cats, as well as from newborn and adult human individuals Krahel (1962) and Heyers (1963) found that this glomus received its blood supply direct from the pulmonary arteries. This finding was based essentially on an assessment of non-injected serially sectioned preparations. That a glomus was in vascular connection with the pulmonary arteries

was supported by the physiological studies of Duke & Green (1964). However, this finding has not been confirmed, neither physiologically (Coleridge, Coleridge & Howe 1970) nor by scrutiny of preparations from adult dogs, cats, rabbits and human beings injected through the pulmonary artery (Coleridge, Coleridge & Howe 1970, Knoche 1966, Verity, Hughes & Bevan 1964).

While, thus, there is some disagreement as to whether the middle aorticopulmonary glomus in fully grown individuals is supplied by the systemic or by the pulmonary circulation, it is beyond doubt that a number of glomera in embryos and young foetuses receive their blood supply from the pulmonary arteries. In human embryos and foetuses the caudal glomera are supplied by a vessel arising from the pulmonary trunk (Muratori 1936, 1937, Palme 1934, Strecht Ribeiro 1945), and in cat foetuses and kittens all glomera were found to be supplied by the pulmonary trunk or right pulmonary artery (Nonidez 1936). In cats, however, the vessel changed its site of origin, at around the time of birth, from the pulmonary to the systemic circulation (Coleridge, Coleridge & Howe 1967, Goormaghtigh & Pannier 1939, Hollinshead 1940c, Hughes 1967, Muratori 1964a, 1965b). In Coleridge, Coleridge & Howe's and in Hughes' materials of perinatal cats the glomera received their blood supply from the pulmonary trunk at birth. In the course of the first 40 days of life anastomoses developed between this glomerular vessel from the pulmonary circulation and glomerular vessels appearing from the systemic circulation. When the kittens were 40 days of age the foetal glomerular vessel from the pulmonary circulation had been obliterated. In newborn dogs there were no pulmonary vessels to the glomera (Coleridge, Coleridge & Howe 1970). In rabbits the upper glomera received, throughout their development, descending arterial branches from the aortic arch, whereas the lower ones, supplied by ascending vessels, changed supply, prior to birth, from the pulmonary arteries to the coronary arteries (Becker 1966a, 1966b). In pigs Schwarz-Karsten (1944) found a pulmonary glomerular artery only during the embryonic period.

In man the vascular supply changes prenatally. The primordium of the inferior aorticopulmonary glomus receives a direct branch from the pulmonary trunk in embryos and early foetuses. At a later foetal stage this vascularization was supplemented by branches from the coronary arteries, especially the left one. After birth the glomic vessel from the pulmonary trunk had completely retrogressed (Boyd 1961). Becker (1966a, 1966b) found—in human foetuses of a fertilization age older than 28 weeks, in newborns, and adults—that the main part of the aorticopulmonary glomera were supplied from an ascending artery (intertruncal artery), arising from the left coronary artery, having anastomoses to branches from the right coronary artery. In a few individuals the upper glomera received very small vessels originating direct from the aorta and anastomosing with the intertruncal artery. In foetuses of a fertilization age between 23 and 28 weeks there was a partially obliterated anastomotic branch between the pulmonary trunk and the intertruncal artery.

The intertruncal artery was of the muscular type, but in the vicinity of the glomera it changed to an elastic type (Becker 1966a). The glomic arteries were equipped with baroreceptive nerve endings (Goormaghtigh & Pannier 1939, Knoche & Schmitt 1963, Nonidez 1937, Seto 1935, Tschernjachiwsky 1938). According to Muratori (1936, 1937) this did not apply to the embryo-foetal vessel from the pulmonary trunk. Boyd (1961) reported that this vessel had a strikingly ample innervation. The glomus arteries penetrated septa in the glomera and entered the lobules in which they divided into a large number of capillaries (Becker 1966a). Goormaghtigh & Pannier (1939) described arterio-venous anastomoses in the organs. They were of the opinion that the intralobular vessels were made up of myoepithelioid cells in the wall, just like the vessels in the coccygeal glomus and in the digital glomera. Similar cells were also found by these authors in the wall of the main arteries. This finding must be compared with that of Knoche & Schmitt (1963) of epithelioid glomus cells (i. e. chief cells) in the wall of the main arteries.

Data concerning venous drainage are scanty. A venous plexus formed around the organs (Becker 1966a, Seto 1935) and presumably emptied into the superior vena cava (Howe 1956, Nonidez 1936).

Inspecting injected and cleared preparations from 40 cats Hughes (1965a) found the aorticopulmonary glomera to receive a small nutritive artery and a large vein draining the tunica media of the pulmonary trunk (*venae vasorum*). After these vessels had passed the glomic sinusoids they emptied into the superior vena cava or the coronary sinus. (A corresponding vascularization system with nutritive and portal afferent vessels was also found in the right and left subclavian glomus, in glomus tissue in the abdomen and along depressor nerves). Hughes did not confirm his glomus findings histologically in all cases. The existence of a portal venous system to the glomera was vigorously denied by Coleridge, Coleridge & Howe (1967), who also used cats, and by Becker (1966a) who used rabbits and human material, and indeed it is not mentioned by Hughes in a subsequent publication (1967) on the vascular supply of the aorticopulmonary glomera. In this latter study he combined the inspection of transilluminated injected whole specimens with that of serially sectioned preparations.

4.1.7. Nerve Supply

On the basis of the morphology and course of the nerves a large number of authors (Boyd 1961, Goormaghtigh & Pannier 1939, Heyers 1963, Muratori 1937, Nonidez 1935, 1936, 1937, Palme 1934, Penitschka 1931, Seto 1935, Strecht Ribeiro 1945) agreed that the main part of the nerves to the glomera were (sensory) fibres from the vagus nerve, only a small part being postganglionic sympathetic fibres. Experiments on cats gave marked support to this assumption (Hollinshead 1940b): The nerves in the aorticopulmonary glomera

degenerated after cutting of the vagus nerve below the inferior ganglion, whereas they remained intact after this nerve was severed cranial to the ganglion. Removal of the superior cervical ganglion had no influence upon the viability of the nerves. Knoche & Schmitt (1963) obtained, especially with a view to the middle aorticopulmonary glomus in cats, dogs, and rabbits, the same results following extirpation of the inferior ganglion of the vagus nerve as Hollinshead (1940b) had obtained by cutting the nerve below the ganglion.

On the basis of a comparison of data supplied by Nonidez (1937), Heyers (1963), Muratori (1965b), and Coleridge, Coleridge & Howe (1970), it must be assumed that the inferior glomera are supplied predominantly by the right vagus nerve, that the middle glomera are supplied equally from the right and left side, and that the superior ones are supplied predominantly by fibres from the left vagus nerve.

In foetuses, newborn infants, and in rabbits (Becker 1966a) bundles of nerve fibres have been found in the connective tissue around the glomera. In infants and rabbits these nerves were myelinated. The interlobular septa contained predominantly non-myelinated nerves whence a nerve plexus of non-myelinated fibres formed around cell clusters. From this plexus issued nerve fibres which between the glomus cells divided into branches partially surrounding the chief cells. Bodian and Bielschowsky's stainings revealed no nerve endings, but by Champy-Maillet's staining bouton-like endings were revealed. In cats Rodríguez Pérez & Ruiz Buitrago (1967), using a similar osmium zinc iodide staining, found that during their course between the glomus cells the nerve fibres showed thickenings ("en passant" synapses), and that they ended in spatulate boutons, partially of an intracytoplasmic situation.

4.1.8. Development

Since most investigations of the development of aorticopulmonary glomera also deal with the development of the subclavian glomus, these glomera will be considered together (please consult section 5.1.8).

4.2. Present Investigations

4.2.1. Site

Within the area of the aorticopulmonary glomera outlined in Fig. 2.1 the following fourteen glomera were found: (1) In each foetus there was a glomus (Fig. 4.1) in the connective tissue between the pulmonary trunk and the ascending aorta, cranial to the origin of the left coronary artery in the aortic bulb. In foetus cr 61 there was, anterior to the main collection a small independent glomus. The above-mentioned glomera will be designated inferior aor-

ticopulmonary glomus cr 55, cr 59, cr 61a, cr 62, and the small one cr 61b. In foetuses cr 55 and 62 the glomus was supplied by a vessel arising from the middle of the pulmonary trunk (Fig. 4.1). (2) In each foetus there was a glomus (Fig. 4.30) situated posteriorly beneath the arch of the aorta in the angle between the arch and the ductus arteriosus, on the right of the latter. This glomus will be called the superior aorticopulmonary glomus cr 55, cr 59, cr 61, and cr 62. (3) Beneath the aortic arch between the inferior and superior aorticopulmonary glomera there were five glomera of a more inconstant situation (Figs. 4.18, 4.30) in relation to the anterior, superior and/or posterior surface of the commencement of the right pulmonary artery. This glomus will be designated the middle aorticopulmonary glomus cr 55, cr 59, cr 61a, cr 61b, and cr 62.

The shape of the cell collections was ovoid, their long axis parallel to the caudal concavity of the aortic arch. The means of the largest transverse diameters were $140 \times 100 \mu\text{m}$ for the inferior aorticopulmonary glomus (this does not include the inferior aorticopulmonary glomus cr 61b which was $45 \times 45 \mu\text{m}$), $140 \times 140 \mu\text{m}$ for the middle aorticopulmonary glomus, and $180 \times 180 \mu\text{m}$ for the superior aorticopulmonary glomus. Presupposing that the glomera were spherical, using the largest transverse measurement as diameter, it was calculated that the aorticopulmonary glomera from a foetus made up a total volume of about one-third of one carotid glomus.

The structure of the aorticopulmonary glomera will be described below together, separate descriptions of the glomera at the three levels, the inferior, middle, and superior aorticopulmonary glomus, appearing in the legends to Figs. 4.2–4.17, 4.19–4.29, and 4.31–4.45.

4.2.2. *Light Microscopy*

In the light microscope (Figs. 4.2, 4.19, 4.31) the organs were found to be made up of cells having oval nuclei with asymmetrically placed nucleoli. The cytoplasm housed small granules and a few major, pale vacuoles. The cell borders were difficult to discern. A few cell nuclei adapted their shape to the neighbouring cells. These adaptive cells were possibly supporting cells. The glomus cells were arranged in dense strands containing thin-walled vessels with irregular lumina. Around the vascular endothelium there were cells whose position suggested pericytes. The cells in the glomus parenchyma had on the whole larger nuclei and more ample cytoplasm than the fibroblasts in the surrounding mesenchyme. In the periphery of the glomera there were frequently thick bundles of nerve fibres and ganglion cells directly adjoining the glomus cells without being separated from them by connective-tissue elements. The fibroblasts around the organs were oriented parallel to the surface, but there was not a question of a true capsule.

4.2.3. *Electron Microscopy*

Whereas from the light microscopic study it was possible to distinguish only tentatively between supporting cells and chief cells in the aorticopulmonary glomera, it was distinctly apparent from the electron microscopic low power view (Figs. 4.3, 4.4, 4.20, 4.32) that such distinction could be maintained. The main elements of the organs were granular cells with a relatively regular nuclear shape as well as non-granular cells with irregular nuclear shape. These two cell types will be designated chief cells and supporting cells respectively.

The chief cells were oval in shape and provided with extensions (Figs. 4.7, 4.8, 4.9, 4.21, 4.34, 4.37). Their nuclei were oval or rod-shaped, but might be notched. The chromatin was delicately granular and irregularly distributed in the nucleoplasm. The chromatin granules formed condensations most of which adjoined the inner nuclear membrane on a level with its areas which did not contain nuclear pores (Fig. 4.6).

The osmiophilic granules in the cytoplasm were striking already at low magnification which set out their extremely varying number per cell area. No polarity was seen in the cells. The granules might be in any part of the cytoplasm. At high magnification (Figs. 4.17, 4.28, 4.45) it was evident that the granules consisted of an electron-opaque homogeneous nucleus surrounded by a cleft of moderate electron opacity and by a membrane. On the basis of measuring the diameters of 1541 specific granules from the aorticopulmonary glomera, the mean was calculated as 118 nm and the standard deviation as 21 nm. 593 granules were from the inferior aorticopulmonary glomera (mean: 122, standard deviation: 20), 519 from the middle aorticopulmonary glomera (mean: 116, standard deviation: 21), and 429 from the superior aorticopulmonary glomera (mean: 114, standard deviation: 20). A statistical description of random samples from an average of 110 granular diameters from each aorticopulmonary glomus is given in Table II.

The electron opacity of the cytoplasm was varied (Figs. 4.7, 4.34). It was not possible to determine whether this variation was due to a varying content and distribution of organelles or to a variation in the electron transparency of the cytoplasmic ground substance. In many cases there was a preponderance of ribosomes in the dark cells. The endoplasmic reticulum was composed of solitary, scattered, flat vesicles, more rarely of aggregates of lamellae lined with ribosomes and of agranular vesicles and vacuoles with pale contents. The ribosomes were not only membrane-bound, but might also occur free in the cytoplasmic ground substance, in the form of solitary granules or in rosettes (Figs. 4.7, 4.8, 4.13, 4.22, 4.28, 4.36, 4.45). The Golgi complex was made up of agranular membranes forming concentric, flat cisterns, vacuoles, and vesicles (Figs. 4.12, 4.13, 4.22, 4.36). A few of the cisterns contained a material of the same electron opacity as that in the nuclei of the specific granules, a phenomenon indicating the formation of granules in the Golgi apparatus (Figs. 4.14, 4.15,

4.26, 4.43). The mitochondria, which were fixation labile, were lying, like the specific granules, apparently scattered haphazardly in the cells. The mitochondria were circular or rod-shaped, with an outer unfolded and an inner folded membrane forming transverse cristae. The intramitochondrial matrix was of moderate electron opacity and occasionally contained mitochondrial granules (Figs. 4.8, 4.13, 4.22, 4.28, 4.36, 4.43). Microtubules occurred scattered in the perikaryon, but were particularly densely arranged in the cellular processes in which they were situated parallel to the long axis of the process (Figs. 4.6, 4.17, 4.22, 4.28, 4.34, 4.36, 4.44). In the chief cells, moreover, there were lysosome-like bodies of varying structure (Figs. 4.14, 4.16, 4.22, 4.26, 4.36, 4.44, 4.45). Centrosome was observed in a few sections. The chief cell plasmalemma did not show any major invaginations or interdigitations with the surrounding cells. The intercellular space was generally very narrow and of constant width (Fig. 4.28). Where two chief cells adjoined there were in limited areas desmosome-like structures at the plasma membranes (Figs. 4.8, 4.29, 4.39). In a few sections there were notches in the plasma membrane, suggestive of micropinocytotic activity and cilia whose tubular pattern in the axial filament complex could not be elucidated (Figs. 4.12, 4.27, 4.40).

The shape of the supporting cells was extremely irregular. Their cytoplasm—and often their nuclei too—adapted their shape to the structures against which they were lying. The chromatin pattern of the nuclei did not differ decisively from that of the nuclei in the chief cells. However, the chromatin condensations were somewhat larger and more numerous. The cytoplasm contained relatively few organelles: Mitochondria, Golgi complex, granular endoplasmic reticulum, free ribosomes, lysosomes, pale agranular vesicles, and occasionally a cilium. It was characteristic of these cells that they gave off long processes which were thin and difficult to trace. The supporting cells invested one or more chief cells (Figs. 4.4, 4.5, 4.20, 4.23, 4.32, 4.33, 4.35), but not always completely. The plasma membrane of the chief cells might be in contact with wide intercellular spaces (Figs. 4.9, 4.23, 4.32, 4.37). Most often, however, the chief cells, when not enveloped by supporting cells, adjoined other chief cells (Figs. 4.7, 4.28, 4.33) or nerve fibres. Other nerve fibres were frequently lying in bundles partially invested by plasma membrane invaginations of the supporting cells. Where nerve fibres and glomus cells adjoined there were none of the structures characteristic of synapses (Figs. 4.4, 4.5, 4.6, 4.16, 4.21, 4.22, 4.23, 4.33, 4.34, 4.38). In many cases there were processes which could not, or not with certainty, be identified as supporting-cell processes, chief-cell processes, or nerve fibres (Figs. 4.21, 4.37).

The vessels were frequently surrounded by perivascular cells, pericytes, which separated the sporadically fenestrated endothelium from the chief cells. The latter might also be separated from the endothelium by supporting-cell processes. It was uncommon to find immediate contact between chief cells and endothelium (Figs. 4.9, 4.10, 4.11, 4.23, 4.24, 4.25, 4.41, 4.42). Around the pericytes and

between groups of chief cells and supporting cells there were collagen fibres and a few fibroblasts.

4.3. Discussion

The division of the glomera beneath the aortic arch into three groups, called here inferior, middle, and superior, is arbitrary. The middle aorticopulmonary glomus cr 62 was in a position corresponding to that in which I found the inferior aorticopulmonary glomus in foetus cr 55. However, since foetus 62 exhibited more caudally a glomus which received its blood supply from the pulmonary trunk, the first-mentioned glomus was assigned to the middle group. The middle aorticopulmonary glomus cr 59 was on immediate inspection (Fig. 4.18) lying in a position in which it might be characterized as a superior glomus, but when considering other survey sections (Fig. 4.30) it must naturally be assigned to the middle group. In foetus cr 61 there was cellular continuity between the glomus of the middle group (61b) which was situated posterior to the right pulmonary artery in the bifurcation of the pulmonary trunk and the superior glomus.

When these findings are compared with Becker's (1966a) description of the localization of glomera in perinatal human individuals, the observations may—in accordance with the appearances in animals (cf. section 4.1.2 and Coleridge, Coleridge & Howe 1967)—be summed up as follows: The aorticopulmonary glomera are made up of a varying number of partially coherent clusters of cells situated within a lambda-shaped figure extending like a strand of varying thickness parallel to the concave under aspect of the aortic arch above the right pulmonary artery from the left coronary artery to the entrance of the ductus arteriosus or the attachment of the ligamentum arteriosum to the aorta, with a process issuing from this site down behind the right pulmonary artery to the right of the ductus arteriosus (ligamentum arteriosum) into the bifurcation of the pulmonary trunk.

In my material the smallest glomus within this area was about $45 \times 45 \mu\text{m}$, the largest one about $180 \times 180 \mu\text{m}$. These sizes make up about 1/3–1/2 of the sizes found by Becker (1966a) in a material of individualt 6–8 months older.

The human aorticopulmonary glomera have not previously been studied by electron microscopy. Compared with the descriptions of their fine structure in animals (section 4.1.4), it is striking that no basal lamina or synaptic structures were found in the human material. However, these discrepancies are presumably due to different stages of development (cf. section 3.3).

My investigation of the fine structure of the carotid glomus and of the aorticopulmonary glomera strongly supports the view advanced on the basis of the general histological and cytological morphology of these organs, viz. that they are of identical structure.

As early as three years before Penitschka (1930, 1931) called attention to the structural similarity of the aorticopulmonary glomera and the carotid glomus, Heymans & Heymans (1927), in physiological experiments, had suggested the existence of chemoreceptors in the chest. This finding was subsequently confirmed and elaborated by int. al. Coleridge, Coleridge & Howe (1967, 1970), Comroe (1939), Gernandt (1946), Neil, Redwood & Schweitzer (1949), and Paintal (1967). For further details the interested reader is referred to reviews by Dripps & Comroe (1944), Neil (1951), Heymans & Neil (1958), and Comroe (1964).

Up to 1965 a total of 28 cases of mediastinal glomus tumours (Smithers & Gowing 1965) and about 500 cases of carotid glomus tumours had been reported (Wilson 1964). However, these numbers should probably be viewed in the light of the fact that the volume of the two carotid glomera is about six times larger than the volume of glomus tissue in the mediastinum.

Subclavian Glomus

5.1. Review of the Literature

5.1.1. *Synonyms for Subclavian Glomus*

Glomus aorticum (Latin: Nonidez 1935).

Paraganglio aortico (Italian: Muratori 1937).

Note that Penitschka (1930) and Nonidez (1935) used this term in a latinized form to designate the aortcopulmonary glomera.

Aortic-arch or fourth-arch bodies (English: Boyd 1937a).

Paraganglio succlavio (Italian: d'Agostini 1953).

Paraganglio or *glomus succlavio* (Italian: Muratori 1960).

Subclavian body (English: Bianconi & Green 1960).

Aortic bodies group 2 + 3 (English: Howe 1956).

Ganglion subclaviare (Latin: Paștea & Paștea 1966).

5.1.2. *Site*

The right subclavian glomus in cats and rabbits lay in the connective tissue of the bifurcation of the brachiocephalic trunk (d'Agostini 1953, Muratori 1934, 1935, 1937, 1962b, Nonidez 1935). In 3 out of 9 cats Howe (1956) found the right subclavian glomus, situated on the ventral side of the root of the right subclavian artery. Hughes (1965a) found the glomus in 3 of 12 cats. In rabbits Palkama & Hopsu (1965) found the organ to be situated 1–4 mm from the bifurcation, on the bisector dividing the angle between the right common carotid artery and the right subclavian artery. In dogs and guinea pigs it was not so well-defined (Muratori 1937, Nonidez 1935, 1937), smaller, and of an extremely varying site, as a rule embedded in the adventitia of the brachiocephalic trunk. In cats and rabbits it was, as also mentioned already, above the right subclavian artery, in dogs and guinea pigs as a rule below this artery. In fine dissection, followed by histological verification, Coleridge, Coleridge & Howe (1970) found a right subclavian glomus in 2 of 23 dogs.

The left subclavian glomus in cats and rabbits has been found on the aortic arch, at the root of the left subclavian artery (Muratori 1934, 1935, 1937, 1962b, Nonidez 1935). In Howe's material of cats a glomus was found on the ventral surface of the aortic arch, at the root of the left subclavian artery in 4 out of 9 cats. 7 of 9 exhibited 1–4 separate groups on the ventral aspect of the aortic arch, caudal to those mentioned above. The glomera were

lying along the left depressor nerve. Similar findings were made by Coleridge, Coleridge & Howe (1967). Hughes (1965a) found a left subclavian glomus in 7 of 12 cats. In dogs (Coleridge, Coleridge & Howe 1970, Nonidez 1937) and guinea pigs (Muratori 1937) the organ was situated caudally on the ventral surface of the aortic arch, on the part of the artery which is between the origin of the left subclavian artery and the ligamentum arteriosum. Coleridge, Coleridge & Howe (1970), in fine dissection with subsequent histological verification, found the glomus in 13 of 23 dogs. On serial sectioning of four relevant specimens they found the glomus in one.

In a muskrat Muratori (1959, 1962c) found on the right two glomera, one above and one below the right subclavian artery, and on the left one in the interstice between the brachiocephalic trunk and the left subclavian artery, immediately above the arch of the aorta. In rats Hollinshead (1941) described very small bodies on both sides, where the recurrent laryngeal nerve arose from the vagus nerve. Nonidez (1935) observed that on the right as well as on the left side the organs were situated in relation to the baroreceptive nerves (depressor or aortic nerve). In addition to the actual subclavian glomera he found smaller glomera, along the main trunks of the nerves as well as peripherally, where the nerves ended in the adventitia in the baroreceptive vascular zones.

In other words, there are fairly consistent descriptions of the site of the subclavian glomus in the most common experimental animals. In man, less definite findings have been made, and the appearances are known only for embryos, foetuses, and neonates. Boyd (1937a) emphasized that the site was greatly varied. In his material of human embryos and foetuses the right glomus was most often situated close to the brachiocephalic trunk, lateral to the trunk in its bifurcation or on the commencement of the right subclavian artery. The left glomus had its site on the aortic arch anteriorly, posteriorly, or medially to the left vagus nerve. Later, Boyd (1961) reported that in a similar material he had found only the left, not the right glomus. In Muratori's material from 1936 the right glomus could not be found. In 1937 he assumed that the "paraganglio cardio-aortico superiore" was homologous to the left subclavian glomus in animals. Tschernjachiwsky (1938) found, in a 20 mm embryo, one glomus below the right 4th brachial arch artery and in a 40 mm embryo five glomera below the arch of the aorta. It cannot be deduced from the description whether the cranial one of these five glomera was so high-lying that it corresponded to the left subclavian glomus. Out of the 56 glomera found by Blessing (1963) in relation to the great vessels in the chest of a four-week-old infant, four were of a position corresponding to that of the right subclavian glomus and about seven in a position corresponding to that of the left subclavian glomus.

The subclavian glomus has not been found in adults (Boyd 1961). The explanation is possibly that with advancing age the small and inconstant glomera are disintegrated by connective tissue as occurs in rabbits (d'Agostini 1953, 1959).

5.1.3. Light Microscopic Structure

Thorough light microscopic descriptions of the organs are not available, the authors restricting themselves to stating that they are made up of epithelioid cells whose appearance and relation to vessels and nerves corresponds accurately to the findings for the carotid glomus. The right subclavian glomus from rabbits has been found to be ovoid, about $600 \times 200 \mu\text{m}$ large, or divided into several small, scattered groups. After haematoxylin-eosin staining a distinction could be made between two types of cell, large round and small spindle-shaped ones (Palkama & Hopsu 1965). In relation to the organs Nonidez (1937) as well as Palkama & Hopsu (1965) found ganglion cells.

5.1.4. Electron Microscopic Structure

Palkama & Hopsu (1965) performed electron microscopic studies on the right subclavian glomus from rabbits following osmium-bichromate fixation. They distinguished chief cells, which were large and whose fine structure was characterized by cigar-shaped mitochondria, large vacuoles, granular endoplasmic reticulum, and numerous membrane-bound granules with electron-opaque nuclei. The diameter of the bordering vesicle was 120 nm. The smaller cells, the satellite cells, were spindle-shaped and invested the chief cells by cytoplasmic extensions. In the cytoplasm there were mitochondria, granular endoplasmic reticulum, numerous agranular vesicles, and fibres of a nature unstated.

Abbott & Howe (1970) studied the left subclavian glomus from cats after glutaraldehyde fixation. They distinguished large type I cells which, apart from the usual organelles, contained characteristic granules. Thin, branched cytoplasmic extensions from type II cells almost completely enwrapped the type I cells. The nerve terminals contained synaptic vesicles, small mitochondria, and glycogen granules adjoined the type I cells. Thickening of the apposed plasma membranes was seen at the sites of contact.

5.1.5. Biogenic Amines

Following fixation by bichromate the cytoplasm of the cells was delicately granular. Chromaffin cells did not occur in the subclavian glomus of rabbits and guinea pigs. Scattered, solitary, chromaffin cells were present in the glomera of cats (Nonidez 1935) and in the muskrat (Muratori 1962c) in which the iodaffin reaction was negative (Muratori 1962b, 1962c). By Tramezzani's ammoniacal silver staining for light microscopic use Muratori, Battaglia & Modonesi (1965a) found only a few or no reacting cells in the right and left subclavian glomera from newborn cats and rabbits. After formaldehyde treatment of the

right subclavian glomus from rabbits Palkama & Hopsu (1965) found greenish fluorescence in the cells.

5.1.6. Vascular Supply

The left subclavian glomus in dogs was supplied by an arterial branch arising direct from the arch of the aorta, ascending aorta, or the neighbouring part of the brachiocephalic trunk (Coleridge, Coleridge & Howe 1970, Nonidez 1937). In cats the artery originated in the commencement of the left subclavian artery, in the root of the brachiocephalic trunk, or in the lateroventral part of the aortic arch (Coleridge, Coleridge & Howe 1967, Howe 1956). The right subclavian glomus was supplied by a small vessel which in the dog arose close to the angle of the brachiocephalic trunk (Coleridge, Coleridge & Howe 1970), in rabbits from the right subclavian artery or brachiocephalic trunk (Nonidez 1935), and in cats close to the root of or from the right subclavian artery (Coleridge, Coleridge & Howe 1967, Howe 1956). From their origin in the great arteries and throughout their course until they reached the respective glomera, the arteries were equipped with baroreceptive nerve endings (Nonidez 1935, 1937). Howe (1956), injecting the vessels in cats, found a venous plexus around the subclavian glomus which drained from both sides to the superior vena cava through one or more small veins.

Each glomic lobule was supplied by its own arteriole which, after having penetrated the connective tissue around the parenchyma, split into numerous capillaries in close contact with the parenchymal cells (Nonidez 1935).

5.1.7. Nerve Supply

In many species of experimental animals the glomera received nerve fibres from the sympathetic trunk (Muratori 1934, 1935, 1965b, Paştea & Paştea 1966) and from the vagus nerve, coursing together with the baroreceptive fibres of the vagus nerve (Muratori 1934, 1935, 1965b, Nonidez 1935, Paştea & Paştea 1966). Hollinshead (1939) performed nerve degeneration experiments on cats. After severing of the vagus nerve below the inferior ganglion, the nerves in the glomera degenerated. However, a few thin, non-myelinated nerves remained intact. Since these, presumably postganglionic autonomic, nerve fibres did not degenerate after removal of the upper cervical ganglion, they could hardly have taken their origin from this ganglion. Severing of the vagus nerve cranial to the inferior ganglion did not result in any changes of the nerves in the subclavian glomus.

The nerves formed a plexus in the connective tissue between the lobules. Hence, the fibres entered the parenchyma where they terminated in contact with the cells (Nonidez 1935).

5.1.8. Development of the Subclavian Glomus and the Aorticopulmonary Glomera

Views on the histogenesis of the thoracic glomera have altered in conformity with the views on the development of the carotid glomus. The origin of these bodies has been ascribed to sympathetic, mesenchymal, and vagal cells.

Rabl (1922), in guinea-pig embryos, found cell groups lying caudally on the neck, lateral to the common carotid artery, on the right extending as far as the base of the heart. On this group of cells he stated: "Sie ist grösser als die Carotisdrüse und stellt einen wohlumgrenzten "chromaffinen Körper" nach der Nomenklatur Kohns dar, dessen Elemente bereits durchwegs von typischem Aussehen sind" (Rabl 1922, p. 323). Studying human embryos Boyd (1937a) found the condensation of cells making up the primordium of the subclavian glomus and the aorticopulmonary glomera to be in very intimate relation to the arteries of the 4th branchial arch and the arteries of the pulmonary arch respectively. From the 13 mm crown-rump stage this primordium was invaded by cells from the vagus nerve and sympathetic trunk, the cells from the latter predominantly to the aorticopulmonary glomera. However, it was difficult to decide on the importance of these nerve-derived cells: "... it is not possible to make a definite statement, as it was when the carotid body was under consideration that such cells are a secondary contribution to a preexisting mesodermal condensation" (Boyd 1937a, p. 27).

Whereas Rabl's and Boyd's studies of the development of the thoracic glomera were secondary to their studies of the carotid glomus, Hammond (1941) performed an extremely thorough study on cats (52 embryos, foetuses, and newborn kittens) with the sole object of clarifying the histogenesis of the subclavian glomus and aorticopulmonary glomera. According to Hammond, the great majority of cells in these glomera were from vagus-derived cells migrating along the depressor nerve. The cells that migrated along the nerve resembled, in the earliest stages, completely those in the sympathetic ganglia. However, they did not stem from these ganglia, since they occurred primarily in large numbers cranial to the anastomoses of the depressor nerve to the sympathetic trunk. During their further development the cells migrated farther caudally, always accompanying the depressor nerve, in order at last to settle in the definitive sites. However, only a very few cells in the final primordium were from the sympathetic trunk. Mesenchymal cells were also not of much importance, only forming the stroma. Vessels came rather late. This is in conformity with Boyd's (1937a) failure to find any vessels in the thoracic glomera of human embryos smaller than about 30 mm in crown-rump length.

d'Agostini (1959) tried to elucidate the development of the subclavian glomus in rabbits. He found a thickening on the artery of the 4th branchial arch which received nerve fibres and cells from the vagus nerve and the cervicothoracic ganglion. He was unable to decide, however, whether the specific cells in

the glomera developed from the nervous or the mesenchymal elements of the primordium. In pig embryos Schwarz-Karsten (1944) excluded that the aorticopulmonary glomera could have been derived from mesenchyme and epithelial cells, but he could not decide whether the cellular material took its origin from sympathetic or parasympathetic cells. According to Boyd (1961) the inferior aorticopulmonary glomus was present in human embryos 20–30 mm in crown-rump length. The primordium consisted of vagus-derived, neuroblast-like cells which together with nerves grew down between the pulmonary trunk and the ascending aorta after fusion of the spiral septum. The primordium was situated in intimate relation to the pulmonary trunk, but there were no signs of preceding thickening of the vessel wall.

5.2. Present Investigations

Within the region of the left subclavian glomus (Figs. 2.1, 5.1) there were, in the four foetuses, seven glomera. Five of them, the left subclavian glomus cr 55, cr 59a, cr 61, cr 62a, and cr 62b, were lying caudally on the left anterior surface of the aortic arch, partially wedged into the groove, opening to the left, between the arch and the ductus arteriosus, in the area anterior to the left vagus nerve (Fig. 5.4). One glomus, the left subclavian glomus cr 62c, was situated cranial to the aortic arch, between the arch and the left vagus nerve (Fig. 5.2) in relation to a thin, vertically coursing nerve (Fig. 5.3). One collection of glomus cells, the left subclavian glomus cr 59b, was 0.5 mm cranial to the origin of the subclavian artery from the aortic arch, behind the left common carotid closely adjacent to a vertically coursing nerve. This nerve continued caudally, in the interstice between the left common carotid artery and the left subclavian artery in which it divided, 0.2 mm above the aortic arch, into two branches that could be traced in the periadventitial tissue to the right and left of the aortic arch.

Within the region of the right subclavian glomus (Figs. 2.1, 5.20) there was, in the four foetuses, one glomus, the right subclavian glomus cr 62. It was lying in the connective tissue about 0.9 mm cranial to the bifurcation of the brachiocephalic trunk, closer to the right common carotid than to the right subclavian artery (Fig. 5.21). It was directly adjoining a well-defined, thin nerve coursing vertically parallel to the right common carotid artery and ending in the nerve plexus at the root of the right subclavian artery.

The size of the eight subclavian glomera ranged from 40 to 150 μ m in diameter. In the light microscope (Figs. 5.3, 5.5, 5.22) they were found to be made up of clusters of poorly delimited cells separated by vessels. The glomera were surrounded by vascular plexuses, bundles of nerve fibres, and often by ganglion cells.

Electron microscopy demonstrated that the architecture of the eight glomera included vessels (except for the left subclavian glomus cr 59b), nerve fibres,

and two cell types, granular chief cells and non-granular supporting cells (Figs. 5.6, 5.7, 5.23, 5.26). The latter often invested chief cells as well as nerve fibres (Figs. 5.8, 5.27, 5.30). By their fine structure, the supporting cells could not be distinguished from Schwann cells in the neighbouring nerves. The chief cells presented with a pale, dark, or intermediately stained cytoplasm (Figs. 5.7, 5.26) which always contained the same organelles: Specific granules (Figs. 5.8, 5.15, 5.26, 5.32), a varying number of ribosomes fairly evenly distributed between the membrane-bound and the free form (Figs. 5.8, 5.12, 5.19, 5.28, 5.29, 5.31), pale agranular vesicles (Figs. 5.11, 5.15, 5.31), mitochondria (Figs. 5.8, 5.19, 5.28, 5.31), Golgi complex not infrequently showing signs of granulogenesis (Figs. 5.8, 5.11, 5.14, 5.28, 5.29), lysosome-like bodies (Figs. 5.12, 5.17, 5.19, 5.26), microtubules, particularly dense in the chief-cell processes (Figs. 5.15, 5.30, 5.32), desmosome-like structures between the plasma membranes of the chief cells (Figs. 5.12, 5.18, 5.19, 5.31), and cilia-like processes (Figs. 5.8, 5.13, 5.28). On the basis of measurements of the diameter (in the vesicle) of 988 specific granules from the subclavian glomera, the mean was calculated to be 112 nm and the standard deviation to be 18 nm. The results of the measurement of each individual glomus are listed in Table II.

The nerve fibres were in non-synaptic contact with the chief cells (Figs. 5.7, 5.8, 5.16, 5.27, 5.30). The chief cells were often separated from the fenestrated endothelium of the vessels by non-granular cells (Figs. 5.9, 5.10, 5.11, 5.24, 5.25). A more detailed description of the left subclavian glomus will be given in Figs. 5.6–5.19, and of the right subclavian glomus in Figs. 5.23–5.32.

5.3. Discussion

In view of the statements in the literature (cf. section 5.1.2) that subclavian glomera are extremely inconstant in man, it seems surprising that in a material of four human foetuses I found no less than eight well-defined aggregations. The difference in the reported findings is presumably due to a question of definition. The five glomera found caudally on the left side of the aortic arch might be classified as the superior aorticopulmonary glomus. In the craniocaudal direction they are situated only a bit cranial to the level of the superior aorticopulmonary glomus. My reasons for including these five glomera among the left subclavian aggregations is that they differ clearly from the superior aorticopulmonary glomus of the foetus in being situated on the left of the aortic arch and the ductus arteriosus. In localization they correspond to Howe's (1956) aortic body group 3.

Apart from these five constantly occurring structures (one in foetus cr 55, one in foetus cr 59, one in foetus cr 61, and two in foetus cr 62) in the junction between the aorticopulmonary and subclavian glomera, I found three subclavian glomera, two on the left side (left subclavian glomus cr 62c, left subclavian

glomus cr 59b), and one on the right (right subclavian glomus cr 62). These three glomera were characterized by an inconstant occurrence and site, being present in only one out of four individuals in the three sites concerned.

They were the three smallest glomera (diameters 40, 45, and 60 μm), and they were situated in immediate relation to vertically coursing, thin nerves. On the basis of the course and relations of these nerves, there might be a question of fibres from the sympathetic trunk (superior and middle cardiac nerves) or vagus nerve (superior and inferior cardiac branches of the vagus nerve and inferior cardiac branches of the recurrent laryngeal nerve) to the cardiac plexus. Together with branches of the vagus nerve (cardiac branches) baroreceptive fibres course to the trunks of the thoracic vessels and chemoreceptive fibres to the thoracic glomera. It is possible, therefore, that the three glomera were lying along baro- and chemo-receptive nerves to the chest.

Although it cannot be ruled out that the glomera were situated along sympathetic fibres, it can be established that neither the three small nor the five glomera in the junctional area could be distinguished from the carotid glomus, in the fine structure of their cells or in the mutual relation between chief cells, supporting cells, nerve fibres, or vessels, or on evaluation of the diameter of the specific granules.

In cats and dogs chemoreceptor activity has been recorded by electrophysiological technique from the baroreceptive nerves to the bifurcation of the brachiocephalic trunk (Bianconi & Green 1960) and to the arch of the aorta (Diamond & Howe 1956), or by recording from the nerves coursing direct to the left and right subclavian glomus (Coleridge, Coleridge & Howe 1967, 1970).

Tympanojugular Glomus

6.1. Review of the Literature

6.1.1. *Synonyms for Tympanojugular Glomus and Sub-divisions*

Gangliolum tympanicum or intumescencia gangliosa r. tympanicum ambiens (Latin: Valentin 1840), cf. section 6.1.2.

Glandula tympanica (Latin: Krause 1878), cf. section 6.1.2.

Glomus jugularis (Latin: Guild 1941).

Glomus jugulare (Latin: Guild 1953, Lattes & Waltner 1949).

Glomus tympanicum (Latin: Zettergren & Lindström 1951).

Glomique tympano-jugulaire (French: Terracol, Guerrier & Guibert 1956).

Tympanic body (English: Capps 1956/57).

Paraganglion temporale or paraganglion ossis temporalis (Latin: Hermanek & Rieder 1964).

Jugulo-tympanic glomus (English: Elliott 1965a).

Paraganglion tympanicum (Latin: Vara-Thorbeck 1970).

6.1.2. *Introduction*

Tympanojugular glomus is the term which I use for the complex of small glomera which have been reported along the auricular branch of the vagus nerve and the tympanic branch of the glossopharyngeal nerve in relation to the adventitia of the superior bulb of the jugular vein and in the middle ear.

Interest in this glomus suddenly increased from the middle of the 1940's when Rosenwasser (1945) described the first recognized case of a carotid glomus tumour-like mass occurring in the middle ear without the simultaneous presence of a carotid glomus tumour. Rosenwasser tentatively suggested: "The possibility that the tumor herein reported may have developed from the glomus jugularis, first named by Guild . . ." (Rosenwasser 1945, p. 67) referring to Guild's preliminary communication from 1941 on the finding of glomera int. al. in the middle ear.

Since that time (cf. Rosenwasser's admirable review from 1968) great efforts have been expended on the study of these tumours. On the other hand, our knowledge of the normal anatomy of the glomera is still limited. Apart from Guild's final paper (1953) which was not published until 12 years after his preliminary communication, there have been only two purely anatomical pub-

lications on the glomera, one on their localization and histological structure (Zettergren & Lindström 1951), and one on their development (Vara-Thorbeck 1970). A few findings of a normal glomus have been reported by authors who have otherwise been concerned mainly with tumours of the tympanojugular glomus (Bartels 1949, Lattes & Waltner 1949), and one finding was made accidentally in a study of the vagal glomus (Watzka & Scharf 1951). In addition to the above-mentioned studies dealing with original glomus findings, reviews have been published by Terracol, Guerrier & Guibert (1956) and Vergés Llardent (1959) and reports of tumours by Capps (1956/57), Hermanek & Reider (1964), and Smith & Gladney (1968) with non-original descriptions and illustrations of the tympanojugular glomus.

After interest was aroused in the tympanojugular glomus owing to its clinical-pathological significance as the origin of otherwise inexplicable neoplastic growths, earlier descriptions of cell findings possibly belonging to this glomus have been unearthed. Chronological reviews on such findings have been given int. a. by Zettergren & Lindström (1951) and by Guild (1953) and will therefore be mentioned here only in brief outline.

One of the most common situations of glomus tissue within the tympanojugular complex is in relation to the commencement of the tympanic branch of the glossopharyngeal nerve (cf. Tables 6.1 and 6.3). In this part of the nerve Valentin (1840) described a spindle-shaped thickening: "Unter dem Mikroskope zeigt diese Substanz die schönsten Ganglienkugeln . . . mit keimblächenartigem Nucleus und dichtem Nucleolus, und von zierlichen Scheiden umgeben, . . ." (Valentin 1840, p. 288). Valentin suggested that this structure be designated *gangliolum tympanicum* or *intumescencia gangliosa r. tympanicum ambiens*. Without referring to Valentin, Krause (1878) described a grossly visible fusiform thickening of the commencement of the tympanic branch of the glossopharyngeal nerve. Microscopically it was richly vascularized, built up of connective tissue and pyramidal or spindle-shaped cells 7–15 μm large with ample cytoplasm "dass schlauchartige Bildungen an die Structur der Gl. intercarotica erinnern" (Krause 1878, p. 738). In accordance with the view prevailing at the time that the carotid glomus was a gland, Krause named the structure tympanic gland. It received its arterial supply from the inferior tympanic artery and its innervation from the tympanic branch of the glossopharyngeal nerve. In the nerves supplying the organ a few small ganglion cells were embedded. Such cells were also found in small groups along the tympanic branch of the glossopharyngeal nerve, but they were not specially accumulated in the part of the nerve where the "gland" was situated (Krause 1879).

Whether the structure called *intumescencia tympanica* in *Nomina anatomica* (1895) represents Valentin's ganglion cells or Krause's gland is uncertain. Although Mulon was unable to study the small "glandes tympaniques" (Mulon 1904, p. 3276) for content of pressor substances, he assigned them, like the

carotid glomus and the adrenal medulla, to the chromaffin system. This view was evidently generally accepted, as text-books referred to the organ as a paraganglion and accordingly it was called "tympanic paraganglion" (Szymonowicz 1930).

In an attempt to elucidate the concepts Watzka (1932)—who gave a critical evaluation of the above-mentioned descriptions—studied 4 human fetuses, 2 newborn infants, 1 adult woman, and 2 guinea pigs. In this material which was not serially sectioned, he found exclusively ganglion cells along the tympanic branch of the glossopharyngeal nerve, "... denn es gibt kein Paraganglion tympanicum und ebensowenig eine Glandula tympanica" (Watzka 1932, p. 249). Later, after finding in the study of the vagal glomus (Watzka & Scharf 1951), in the wall of the superior bulb of the jugular vein in a 40-year-old man, a non-chromaffin paraganglion, whose structure and cells corresponded in every respect to the "paraganglion caroticum", he was not so categorical in rejecting the early workers' findings.

According to the microscopic descriptions it seems most likely that the structure described by Valentin was an accumulation of ganglion cells which indubitably occur along the tympanic branch of the glossopharyngeal nerve (Bötner 1959). On the other hand, I consider it extremely likely that the structures described by Krause were in fact glomera, as they correspond, according to Krause's description—with respect to situation, morphology, vascularization, and innervation—accurately to subsequent findings. Guild (1953), who published his preliminary results as early as 1941, referring to a text-book figure (Krause 1879) which in fact corresponds very inadequately to the original verbal description (Krause 1878), believed that what Krause described was nothing but connective tissue in the tympanic canaliculus. Thus, there is some uncertainty as to who first described the tympanojugular glomus, but there is no doubt who has contributed most to our knowledge of their anatomy: S. R. Guild.

When disregarding the questionable early findings, I have come across in my perusal of the literature reports on the finding of about 310 tympanojugular glomera. They are listed, with sources stated, in Table 6.1. It should be mentioned that I have not found any reports on a tympanojugular glomus in animals.

6.1.3. Site and Occurrence

Guild's material from 1953 is the only one of those listed in Table 6.1 which is of a size that permits a more detailed analysis of the distribution of the glomera, and it will therefore be reviewed in some more detail.

Guild's material comprises both otic capsules from 44 persons. The bones were fixed in formalin, decalcified, and cut into serial sections 24 μ m thick. Every 10th section, sometimes every 5th, was stained with haematoxylin-eosin.

Table 6.1. The reported findings of tympanojugular glomus. In 117 specimens from human individuals of all ages and of both sexes about 310 glomera have been found, i.e. an average of about 2.7 glomera per temporal bone. About half the glomera were situated along the tympanic branch of the glossopharyngeal nerve, and about half along the auricular branch of the vagus nerve in the superior jugular bulb. Comment: (a) The numerical values are calculated on the presupposition that Vara-Thorbeck studied only one temporal bone from each individual of his material.

No. of glomera	No. of specimens	Age distribution	Sex ratio	Average No. of glomera per specimen (range)	Site of glomera	Author
248	88	12: 8–19 yrs. 52: M 54: 20–59 yrs. 36: F 22: 60–79 yrs.		2.82 (0–12)	135: Along tympanic branch of glossophar. nerve 113: Along auricular branch of vagus nerve (more detailed distribution in Tables 6.2 and 6.3)	Guild 1953
ca. 45	15	12: fetuses 3: newborns	15: ?	ca. 3 (1–4)	Along tympanic branch of glossophar. nerve ca. 22: infratympanic ca. 11: intratympanic ca. 11: supratympanic	Vara-Thorbeck 1970 ^a (pp. 474–477)
10	10	2: 30–32 yrs. 8: 62–88 yrs.	7: M 3: F	1 (0–2)	Along tympanic branch of glossophar. nerve 6: infracanalicular 3: intracanalicular 1: on promontory	Zettergren & Lindström 1951 (Table 1 and Fig.7)
3	1	1: adult	1: ?	3	1: wall of sup. bulb of jug. vein 1: in tymp. canaliculus 1: on promontory	Lattes & Waltner 1949, p. 463; Figs. 14–15 Figs. 16–17
2	1	1: 7 yrs.	1: M	2	2: wall of sup. bulb of jug. vein	Figs. 18–19 Figs. 20–21
1	1	1: 40 yrs.	1: M	1	1: wall of sup. bulb of jug. vein near inf. vag. ganglion	Watzka & Scharf 1951, p. 142
1	1	1: ?	1: ?	1	1: wall of sup. bulb of jug. vein near tymp. branch of glossophar. nerve	Bartels 1949, p. 17

In the 88 bones studied he found 248 glomera, 135 of which were situated along the tympanic branch of the glossopharyngeal nerve and the remaining 113 along the auricular branch of the vagus nerve. The number per temporal bone ranged from 1 to 12, average 2.82 in each bone. In 5 bones no glomera were found, but small glomera may have been hidden between the studied sections. The glomera exhibited bilateral uniformity with respect to number and situation. Race, sex, and side of head had no influence upon the occurrence of the glomera, whereas age was of importance. The largest number per bone was found in middle-aged persons (30–50 years), fewer in children, adolescents, and elderly persons.

As is apparent from Table 6.2, no less than 50 % of all glomera were situated in the jugular fossa, 12 % in the middle ear, and the remaining 35 % in the bony canals.

Table 6.3 shows that glomera were found along any part of the tympanic branch of the glossopharyngeal nerve, from its origin in the glossopharyngeal nerve to its continuation as the lesser petrosal nerve. Of the 135 glomera along the tympanic branch of the glossopharyngeal nerve 14 were close to the origin of the nerve, 37 along its course in the adventitia of the superior bulb of the jugular vein, 54 along the relatively short part in the tympanic canaliculus, and 30 in the middle ear, the majority in the tympanic plexus on the promontory.

Of the 113 glomera along the auricular branch of the vagus nerve 81 were along the course of the nerve over the superior bulb of the jugular vein, the majority along the posterolateral part of the nerve, 25 in the mastoid canaliculus in a corresponding extracranial groove; the remaining 7 were situated along the course of the nerve in the descending facial canal.

6.1.4. Light Microscopic Structure

According to Guild (1953) a typical glomus was ovoid, 0.25×0.5 mm, but it might vary in size from 0.1 to 1.5 mm. Very small glomera may have been overlooked, as there were 0.24 mm between the studied sections. One-fifth of the glomera were 0.25×0.5 mm, one fifth larger, and three-fifths smaller. The glomera were made up of small blood vessels adjoining epithelioid cells and were surrounded by a connective-tissue capsule. The larger ones were divided into several lobules by connective-tissue septa. According to whether the vessels or the intervacular cells predominated, Guild made a distinction between two histological types: Vascular glomera which made up about 30 % and cellular glomera which made up about 70 %. In the same temporal bone glomera of one type predominated, whereas the two bones from the same person might be characterized each by its histological type. By age, sex, and number of glomera per ear there was no significant difference in the distribution of the two types.

Table 6.2. Distribution of tympanojugular glomera. Site of glomera in relation to the bony structures in the temporal bone. Table based on data given by Guild (1953) in his text.

		Number of glomera	Distribution of glomera in per cent
Glomera belonging to the tympanojugu- lar glomus	In jugular fossa	132	53
	In tympanic canaliculus	54	22
	In labyrinthine wall	30	12
	In mastoid canaliculus	25	10
	In facial canal	7	3
Total		248	100

Table 6.3. Distribution of tympanojugular glomera. Site of glomera given in relation to tympanic branch of the glossopharyngeal nerve and auricular branch of the vagus nerve. Table based on data given by Guild (1953) in his text.

			Number of glomera	Distribution of glomera in per cent
Glomera belonging to the tympano- jugular glomus: 248	Glomera along tympanic branch Number: 135 Share: 54 %	Close to origin of nerve	14	6
		In adventitia of sup. bulb of jug. vein.....	37	15
		In tympanic canaliculus	54	22
		In submucosa on the promontory	30	12
	Glomera along auricular branch Number: 113 Share: 46 %	In adventitia of sup. bulb of jug. vein.....	81	33
		In mastoid canaliculus.	25	10
		In facial canal	7	3
	Total		248	ca. 100

According to Zettergren & Lindström (1951) a typical glomus was round or ovoid, diameters $0.28-0.38 \times 0.15-0.18 \times 0.2$ mm. A few glomera were divided by thin collagen connective-tissue septa into two lobules. The glomera were predominated by tortuous capillaries, precapillary vessels, and epithelioid cells. The nuclei of these cells were of uniform size, round or oval, with a very

loose and delicate chromatin structure. The cytoplasm was ample, and occasionally there was delicate eosinophil granulation.

The glomus found by Bartels (1949) was made up of large cells with ample cytoplasm and dark nuclei, but owing to the thickness of the sections it is not possible to assess the structure with accuracy.

6.1.5. Biogenic Amines

The few investigations done to elucidate the chromaffinity of the glomera have disclosed that the cells are non-chromaffin. They have comprised a bichromate-formalin fixed specimen from a 7-year-old boy showing two non-chromaffin glomera in the superior bulb of the superior jugular vein (Lattes & Waltner 1949), a bichromate-formalin fixed specimen from a 40-year-old man showing one non-chromaffin glomus in the bulb of the superior jugular vein (Watzka & Scharf 1951), and specimens from three newborns (presumably about 9 glomera, cf. section 6.1.8), prepared by the method of Schmorl in which glomera along the tympanic branch of the glossopharyngeal nerve were non-chromaffin (Vara-Thorbeck 1970).

6.1.6. Vascular Supply

According to Guild (1953) the vessels to the glomera originated from the inferior tympanic artery coming from the ascending pharyngeal artery coursing along the tympanic branch of the glossopharyngeal nerve and giving off a small branch accompanying the auricular branch of the vagus nerve. Zettergren & Lindström (1951) also found the source of supply to the glomera situated along the tympanic branch of the glossopharyngeal nerve to be the inferior tympanic artery.

6.1.7. Nerve Supply

According to Guild (1953) the glomera are almost exclusively innervated by non-myelinated nerves. The number of fibres was large compared to the size of the organs. By silver staining it was demonstrated that these numerous nerves coursed between the epithelioid cells, but by the technique used it was not possible to observe synapses.

Depending on the situation of the glomera the nerve fibres coursed to the organs in the tympanic branch of the glossopharyngeal nerve and auricular branch of the vagus nerve respectively. Guild could not rule out that the nerve fibres which innervated glomera situated along the auricular branch of the vagus nerve coursed in the communicating branch of the vagus nerve with the glossopharyngeal nerve, so that the original source was the glossopharyngeal nerve.

6.1.8. *Development*

Griffith & Boyd (1959) reported that by serially sectioning a large number of human embryos and fetuses, all smaller than 150 mm in crown-rump length, they found no glomus tissue belonging to the tympanojugular glomus. A similar negative result was reported by Vara-Thorbeck (1970) in embryos and fetuses smaller than 125 mm in crown-rump length. Vara-Thorbeck serially sectioned human paraffin-embedded temporal bone specimens from 3 embryos, 12 fetuses, and 3 neonates with a view to elucidating the development and course of the tympanic branch of the glossopharyngeal nerve. It is not apparent from the paper whether the investigation comprised temporal bones from both sides of the head or just from one.

Within the material there were, in individuals larger than or equal to 125 mm crown-rump length, up to four separate glomera in relation to each tympanic branch of the glossopharyngeal nerve. Along the infratympanic course of the nerve there were 1–2 relatively large (in the range 0.6 mm) glomera, along its intratympanic course 0–1 relatively small ones (about 0.2 mm), and along its supratympanic course 0–1 moderately large (0.4 mm) glomera. The relation between the tympanic branch of the glossopharyngeal nerve and the glomera was extremely intimate in all cases. The very small glomera situated in the tympanic wall were often completely embedded in the nerve. Frequently they were close to sites where the tympanic branch of the glossopharyngeal nerve or the lesser petrosal nerve received anastomotic branches from the internal carotid plexus and the facial nerve respectively.

The glomera were surrounded by a connective-tissue capsule which rarely gave off lobule-forming septa, and contained a pronounced vascular meshwork of capillaries, sinusoids, and venules. In the parenchyma two types of cell were observed, each showing a certain variation in size and appearance. It was characteristic of one type that the cells were rather large and round, with ample cytoplasm and a nucleus high in chromatin. The other type was characterized by smaller, longish, or semilunar cells with spindle- or egg-shaped chromatophil nucleus. On the basis of the appearance of the cells Vara-Thorbeck assumed that the former type represented neuroblasts derived from the glossopharyngeal nerve, in different stages of differentiation and the latter type mesoblasts.

6.2. Present Investigations

The tympanojugular glomus was sought in specimens consisting of the jugular foramen with adjacent bones (Fig. 6.1) from the right and left side of the heads of fetuses cr 55, 61, 62, and from the right side of foetus cr 59. The direction of sectioning through the preparations was in all cases by approximation parallel to the posterior surface of the petrous portion of the temporal bone. This direction of sectioning afforded a good possibility of searching the bulb of the

Table 6.4. Characteristics of the preparations stepwise sectioned to look for the tympano-jugular glomus. The tympanic branch of the glossopharyngeal nerve and the auricular branch of the vagus nerve were traced from their origin in the respective cranial nerves. The fractions of the nerves' peripheral course given in the table are based on an estimate. In this characteristic no regard is paid to the removal of small pieces of the nerves in shaping the ultrapyramids (cf. Table 2.3).

	Foetus cr 55 R. side	Foetus cr 55 L. side	Foetus cr 59 R. side	Foetus cr 61 R. side	Foetus cr 61 L. side	Foetus cr 62 R. side	Foetus cr 62 L. side
Stepwise sectioned depth, mm	0.9	1.2	0.8	0.4	1.2	2.0	2.3
Stepwise sectioned parts (in frac- tions) of the auricular branch and	medial 1/4 in jugular fossa	medial 1/3 in jugular fossa	none	medial 1/3 in jugular fossa	medial 1/2 in jugular fossa	1/1 in jugular fossa 1/1 in mastoid canali- culus 1/2 in facial canal	1/1 in jugular fossa 1/1 in mastoid canali- culus 2/3 in facial canal
the number of glomera found along or close to the branch	1	0	0	0	0	2	2
Stepwise sectioned parts (in frac- tions) of the tympanic branch and	none	none	1/1 infra- tympa- nic 2/3 intra- tympa- nic	1/1 infra- tympa- nic	none	1/1 infra- tympa- nic 2/3 intra- tympa- nic	1/1 infra- tympa- nic 1/2 intra- tympa- nic
the number of glomera found along the branch	0	0	1	0	0	1	1

superior jugular vein and of tracing the tympanic branch of the glossopharyngeal nerve and the auricular branch of the vagus nerve from their origin in the cranial nerves. The searched areas are listed in Table 6.4.

An impression of the course of the nerves and other anatomical features may be obtained by studying the low magnification shown in Figs. 6.2, 6.4, 6.6, 6.8, 6.10, 6.12, 6.14, and 6.16. Although these figures represent different foe-

tuses and sides of the head, they are arranged so that apparently they make up a selection of a series sectioned through one preparation.

The auricular branch of the vagus nerve originated by several roots (Figs. 6.2, 6.6) from the areas between the inferior and superior ganglia of the vagus and glossopharyngeal nerves. At a rough estimate two-thirds of the fibres took their origin in the vagus and one-third in the glossopharyngeal nerve (communicating branch of the vagus nerve with the glossopharyngeal nerve). There were marked variations in the number of roots, their origin in the cranial nerves, their initial course and junction. Most roots, however, joined a short distance after their origin. In this way the main stem of the auricular branch of the vagus nerve was formed. It coursed laterally in the mesenchyme of the jugular fossa, between the superior bulb of the jugular vein and the floor of the middle ear (Figs. 6.4, 6.6, 6.8, 6.14). The medial part of the nerve was embedded periadventitiously in the wall of the jugular vein (Figs. 6.4, 6.6, 6.8), whereas its lateral part moved farther and farther from the venous wall (Fig. 6.14) coursing towards the mastoid canaliculus (Fig. 6.10) which in the foetuses showed the appearance of a wide canal. The nerve passed through the mastoid canaliculus in the facial canal (Fig. 6.12) which it crossed, exchanging fibres with the facial nerve.

The tympanic branch of the glossopharyngeal nerve originated in one stem from the inferior ganglion of the glossopharyngeal nerve (Fig. 6.4), whence it coursed forward and laterally in the mesenchyme between the medial part of the superior bulb of the jugular vein and the floor of the middle ear (Fig. 6.6), i. e. in the same position as and almost parallel to the commencement of the auricular branch of the vagus nerve, only more caudally. Hence it continued through the medial part of a wide foramen, the future tympanic canaliculus (Fig. 6.8), into the future middle-ear cavity which at the foetal stage was largely filled with loose, peritympanic connective tissue. The nerve was embedded in the perichondral connective tissue on the promontory (Fig. 6.17), i. e. on that part of the periotic capsule around the basal cochlear turn which projected into the middle-ear mesenchyme (Figs. 6.10, 6.12, 6.14, 6.16). In relation to these nerves and/or the superior bulb of the jugular vein the following eight, major well-defined glomera were found:

Tympanojugular glomus cr 55:

An accumulation of cells, about $40 \times 20 \mu\text{m}$, partially embedded in the largest root of the auricular branch of the vagus nerve, situated medially in the jugular fossa, in the area between the cranial nerves, the superior bulb of the jugular vein and the floor of the tympanic cavity. The accumulation was in no immediate contact with vessels. Apparently it did not contain any independent supporting cells, but its chief cells were surrounded on all sides and partially separated mutually by cells and cell processes which acted at the same time as Schwann cells for the axons in the auricular branch of the vagus nerve.

(Illustrations: Light microscopic Figs. 6.2, 6.3, electron microscopic Figs. 6.19, 6.30).

Tympanojugular glomus cr 59:

An accumulation of cells, about $30 \times 30 \mu\text{m}$, partially embedded in the tympanic branch of the glossopharyngeal nerve situated along the intratympanic course of this nerve in the mesenchyme between the promontory and the primitive middle-ear cavity. The glomus was separated from the nerve trunk by a narrow connective-tissue space, and in its remaining circumference it adjoined thin-walled vessels whose endothelium did not appear to contain fenestrae. On electron microscopy it was possible to distinguish chief cells, supporting cells, and nerve fibres. (Illustrations: Light microscopic Figs. 6.16, 6.17, electron microscopic Figs. 6.20, 6.27, 6.33, 6.34, 6.38, 6.39).

Tympanojugular glomus cr 62a:

An accumulation of cells, about $60 \times 60 \mu\text{m}$, situated about $300 \mu\text{m}$ peripheral to the origin of the tympanic branch from the inferior ganglion of the glossopharyngeal nerve, i. e. approximately midway in the infratympanic course of the nerve in the medial, smaller part of the jugular fossa. The accumulation, arranged around vascular lumina, consisted of chief and supporting cells adjoining nerve fibres. Small ganglion cells were observed in the vicinity of the glomus. (Illustrations: Light microscopic Figs. 6.4, 6.5, electron microscopic Figs. 6.25, 6.26, 6.40).

Tympanojugular glomus cr 62b:

An accumulation, about $60 \times 60 \mu\text{m}$, in relation to the tympanic branch of the glossopharyngeal nerve immediately before the nerve entered the tympanic canaliculus. This group of cells, whose fine structure was not investigated because of an error on the author's part, was surrounded by thin-walled vessels. (Illustrations: Light microscopic Figs. 6.6, 6.7).

Tympanojugular glomus cr 62c:

An accumulation about $40 \times 20 \mu\text{m}$, partially split by a vascular lumen into two parts, situated in the middle of the jugular fossa, wedged in between the auricular branch of the vagus nerve and the wall of the internal jugular vein. This glomus was built up of nerve fibres, chief cells, supporting cells, and vessels with endothelial pores. (Illustrations: Light microscopic Figs. 6.8, 6.9, electron microscopic Figs. 6.18, 6.31, 6.32, 6.36, 6.37).

Tympanojugular glomus cr 62d:

A glomus, about $60 \times 30 \mu\text{m}$, situated lateral to the jugular fossa, periaventritially in relation to the superior bulb of the jugular vein. This group of

chief and supporting cells was not particularly amply vascularized. Electron microscopy disclosed that the glomus contained numerous nerve fibres. In the light microscope it was not possible to ascertain whether these fibres originated in the auricular branch of the vagus nerve which coursed at a distance of 100–200 μm from the glomus. (Illustrations: Light microscopic Figs. 6.10, 6.11, electron microscopic Figs. 6.28, 6.29).

Tympanojugular glomus cr 62e:

An amply vascularized glomus, about $80 \times 40 \mu\text{m}$, situated periadventitally in the superior bulb of the jugular vein, between the vessel wall and the tympanic floor. In relation to the jugular foramen the organ was situated in the sagittal plane through the junction of the medial two-thirds and the lateral one-third of the jugular fossa. In this sagittal plane the auricular branch of the vagus nerve was situated about 215 μm to the cranial aspect, on the anterior surface of the superior bulb of the jugular vein. Despite this distance between the auricular branch of the vagus nerve and the glomus, the glomus contained nerve fibres. The origin of these fibres could not be traced. (Illustrations: Light microscopic Figs. 6.12, 6.13, electron microscopic Figs. 6.21, 6.22).

Tympanojugular glomus cr 62f:

A glomus, about $60 \times 40 \mu\text{m}$, situated periadventitally in the anterior wall of the superior bulb of the jugular vein, approximately midway between its medial and lateral border. The cluster of cells was lying caudal to the site where the auricular branch of the vagus nerve left the bulbar wall. The glomus was made up of chief and supporting cells, vessels, and nerves. (Illustrations: Light microscopic Figs. 6.14, 6.15, electron microscopic Figs. 6.23, 6.24, 6.35).

Summing up the localization of the eight tympanojugular glomera, it may be said that three were situated in relation to the tympanic branch of the glossopharyngeal nerve, one in its course between the inferior ganglion of the glossopharyngeal nerve and the tympanic canaliculus, one at the entrance to the tympanic caniculus, and one on the promontory in the middle ear. Two glomera were situated in immediate relation to the auricular branch of the vagus nerve, and three periadventitally in the superior bulb of the jugular vein without contact with the auricular branch of the vagus nerve.

As to the structure, certain differences were found, especially with respect to the degree of vascularization. For instance, tympanojugular glomus cr 55 did not contain any vessels, whereas tympanojugular glomera cr 62a and 62e had a vascular network well-developed as compared to their cellularity. Electron microscopy disclosed in the vascular glomera endothelial pores only in tympanojugular glomera cr 62a, 62c, 62e, and 62f. Rare fine structures were not demonstrated in each individual glomus, e. g. cilia were seen only in tym-

panojugular glomera cr 62a and 62c. When these differences are borne in mind, the fine structure of the glomera may be described under the same heading.

The glomera were made up of vessels, nerve fibres, and two types of cells, granular chief cells and non-granular supporting cells (Figs. 6.18, 6.19, 6.20, 6.21, 6.23, 6.25, 6.27, 6.28). The nucleus of the supporting cells was irregular, often semilunar, and relatively dark (Fig. 6.27), surrounded by a narrow rim of perinuclear cytoplasm containing a small Golgi zone and a few ribosomes as well as mitochondria. It was characteristic of this type of cell that it gave off thin cytoplasmic extensions embracing chief cells and/or nerve fibres (Figs. 6.18, 6.19, 6.27, 6.28). The supporting cells were not distinguishable by their fine structure from Schwann cells in neighbouring nerves (cf. Figs. 6.18, 6.19).

The nucleus of the chief cells was usually rounded and ovoid (Fig. 6.27), but occasionally exhibited deep notches (Fig. 6.19). The chromatin fragments were irregularly distributed, so that the nucleus had a patchy appearance. The chromatin fragments always accumulated beneath the nuclear membrane (Fig. 6.31) and close to nucleoli (Fig. 6.27). The nucleus was surrounded by a perinuclear cistern whose inner portion embraced the peripheral chromatin condensation closely and whose outer portion sometimes gave off extensions into the cytoplasm, forming agranular endoplasmic reticulum (Fig. 6.30). The perinuclear cistern was closed in punctate spots by nuclear pores (Figs. 6.30, 6.31). The mitochondria were oval or rod-shaped with transversely placed crests and a few granules in the matrix (Figs. 6.31, 6.35). At times the mitochondria were swollen. The rough endoplasmic reticulum was scanty, occurring partly in the form of solitary, flat vesicles and partly as a few parallel lamellae, occasionally with branchings. Similar small vesicles and lamellae had no ribosomes attached to their outer surface (Figs. 6.31, 6.33, 6.35, 6.38). Non-membrane-bound ribosomes occurred in major numbers, usually collected in small groups (Figs. 6.32, 6.34, 6.35, 6.38).

The Golgi complex was well-developed and lying in a perinuclear situation in the vicinity of the cytocentre. It was built up as a horseshoe-shaped structure, consisting of 3–8 cisterns arranged in parallel rows, several vacuoles, and numerous vesicles (Figs. 6.29, 6.31, 6.33, 6.34, 6.35). Golgi vesicles were on the whole smaller than the vesicles of the specific granules, whereas the vacuoles were larger. At the terminal end of Golgi cisterns there were occasionally accumulations of an electron-opaque material of a nature like the core of the specific granules (Figs. 6.31, 6.34). Scattered in the cytoplasm there were many vesicles and vacuoles which could not be definitely identified (Figs. 6.31, 6.32, 6.33, 6.34). The electron opacity of the content in these membrane-bound areas varied from completely transparent to the same density as the cytoplasmic ground substance. The electron density of the latter varied from cell to cell (Figs. 6.18, 6.25).

In electron microscopic low power views the specific granules stood out as

dark, irregularly distributed dots in the cytoplasm of the chief cells (Figs. 6.19, 6.20). In high power views it was possible to discern a vesicle with trilaminar membrane (Fig. 6.36) which at some distance surrounded an electron-dense, almost homogeneous, central core (Fig. 6.34). The granules showed quite some variation in appearance (Figs. 6.39, 6.40) and size. The mean diameter in 837 granules measured was 114 nm, standard deviation 21, 95 % interval 74–154 nm. A description of the random samples from each tympanojugular glomus is given in Table II. The cytoplasm contained lysosome-like bodies of different types (Figs. 6.31, 6.33, 6.35). The satellites in the centrioles were anchored by microtubules (Figs. 6.33, 6.37). Microtubules were also observed singly, longitudinally or transversely sectioned, in the juxtannuclear cytoplasm (Fig. 6.32). Cilia of a $9 \times 2 + 0$ structure (Fig. 6.32) were observed in a very few cells (Fig. 6.31) in whose cytoplasm they were deeply invaginated. The plasma membrane of the cells occasionally exhibited signs of micropinocytotic activity (Fig. 6.39). Where two chief cells adjoined, desmosome-like structures might occur (Figs. 6.29, 6.30, 6.36, 6.38).

In all glomera nerve fibres were prominent. Major bundles were observed even in low power views (Figs. 6.18, 6.20, 6.23, 6.28), and at higher magnification numerous nerve fibres were seen to be wedged in between chief and supporting cells (Figs. 6.26, 6.27, 6.29, 6.36, 6.39).

The exact mutual relation between chief cells, supporting cells, and nerve fibres was difficult to interpret, especially in areas predominated by cell processes (Fig. 6.20). This was due partly to the intricate architecture and partly to the constant presence of cell processes which were difficult to identify. As a main rule, chief cells either adjoined other chief cells or else were surrounded by thin, non-granular cell processes. It was only in very limited areas that the plasma membrane of the chief cells was in direct contact with the endothelium of the vessels (Fig. 6.21), nerve fibres, or with wide intercellular spaces (Figs. 6.18, 6.24).

The glomic vessels consisted of a thin layer of endothelial cells, partially surrounded by perivascular cells (Figs. 6.21, 6.23, 6.25). The endothelium contained series of fenestrae (Figs. 6.22, 6.24, 6.26). The vascular lumina were often separated from the chief cells by pericytes as well as by supporting cells, but a closer contact might also occur (Fig. 6.21).

6.3. Discussion

According to Guild (1953) there are 2.82 glomera per temporal bone, a little more than half (54 %) along the tympanic branch of the glossopharyngeal nerve (cf. Table 6.3). In my foetal material of seven specimens of temporal bones, glomera were relatively few, on the average about 1 (1.1) per prepara-

tion, less than half (3/8) along the tympanic branch of the glossopharyngeal nerve.

The explanation of these discrepancies is that the glomera described in my material represent, for the reasons stated below, absolute minimum values for glomera in each temporal bone:

(1) All questionable findings were excluded from the material. The primary object of my studies was to ascertain whether there are in the superior bulb of the jugular vein or along the tympanic branch of the glossopharyngeal nerve any formations of an architecture like the carotid glomus. I, therefore, excluded findings which because of too small size or technical difficulties did not afford sufficient material for morphological analysis.

(2) By trimming the blocks with a view to ultra-sectioning, tissue has been cut off areas of the embedded preparations which may have contained glomus.

(3) My preparations are not optimally suited for mapping the presence of glomera. Their suitability with a view to searching glomera is assessed in Table 6.4. The varying suitability is due essentially to the delicate work in cutting out the specimens which gave rise to different delimitation and varying traumatization of the tissue. The main reason why I found a fairly low average number of glomera per preparation was that the preparations always contained only part of the areas within which glomera may theoretically occur. The findings of relatively few glomera along the tympanic branch of the glossopharyngeal nerve were due to the area of the tympanic branch being most poorly represented. As might be expected, the largest number of glomera were found in the optimal preparations from foetus cr 62.

The light microscopic structure of the tympanojugular glomus from foetuses has been described by Vara-Thorbeck (1970). When considering that Vara-Thorbeck's investigations were on paraffin sections and mine on semi-thin epoxy resin sections, Vara-Thorbeck's neuroblastic cells presumably correspond to my chief cells and his mesoblastic cells to my supporting cells and pericytes. In Vara-Thorbeck's material the glomera contained a well-developed vascular network, whereas in my material the vascularization differed from glomus to glomus. This discrepancy may be of developmental nature, the glomera in Vara-Thorbeck's material being derived from older individuals than the glomera of my material. At least, the glomera increase in size with age. In my material the glomera from small foetuses (crown-rump length about 60 mm) were 20–80 μm , in Vara-Thorbeck's material from larger foetuses (crown-rump length more than 125 mm) 100–600 μm , and in Guild's material (1953) from adults 100–1500 μm .

The differences in the vascularity of my glomera may be due to the glomera, as early as the immediately postembryonic developmental stage, having differentiated into "vascular" and "cellular" types which according to Guild occur in adults. In that case, the continued development after the early foetal stage ought to be restricted to simple increase in size.

To my knowledge, electron microscopic studies of the tympanojugular glomus have not been published previously. Smith & Gladney (1968) tried, with a view to electron microscopic comparison of normal glomus with tympanojugular glomic tumours, to isolate the normal glomus from the jugular fossa of a cadaver, but failed owing to the small size of the structure and its inconstant site.

On the other hand, at least 14 tumours believed to have arisen from this glomus have been subjected to electron microscopy (Balogh, Draskóczy & Caulfield 1966, Boyd, Lever & Griffith 1959, Gejrot, Lagerlöf & Wersäll 1964, González-Angulo, Fería-Velasco, Corvera & Elias 1968, Kawabata, Duvall & Paparella 1969, Seifert 1965, Smith & Gladney 1968). All the tumours were predominated by a cell containing osmiophilic granules. These granules were compared with granules in the carotid glomus, in sympathetic nerves, in the adrenal medulla, in argentaffin cells, in Merkel cells, in malignant melanomas, in carotid glomus tumours, and in tumours arising from the adrenal medulla. It should be mentioned that the granules in the abnormal tympanojugular glomus cells were in several cases of the reported studies compared with the granules of normal cells, a factor which highly restricts the value that can be attached to the conclusions drawn concerning the type of cell from which the tumours have originated. It must be expected that the granular size (and number) may differ in normal and in abnormal, dedifferentiated tumour cells, as has been demonstrated for normal cells of the adrenal medulla (pheochromocytes) and those of adrenal medullary tumours, pheochromocytomas (Yokoyama & Takayasu 1969).

Boyd, Lever & Griffith (1959) pointed out such a marked discrepancy between the time at which the carotid glomus and the tympanojugular glomus is laid down that the two organs cannot be considered homologous. The first visible sign of the carotid glomus appears in human embryos 13–16 mm in crown-rump length (Boyd 1937a). On serial sectioning of paraffin-embedded preparations Griffith & Boyd (1959) as well as Vara-Thorbeck (1970) failed to find the tympanojugular glomus in fetuses and embryos smaller than 150 and 125 mm respectively in crown-rump length. However, these results are subject to some doubt. In thin plastic sections I identified glomera in very small fetuses, and this opens up the possibility that glomus cells belonging to the tympanojugular glomus do in fact appear at the embryonic stage. Only, the very small accumulations, presumably smaller than 20 μm , cannot be disclosed and identified in a study of the relatively thick paraffin sections.

To elucidate the certainty with which the tympanojugular glomus may be considered structurally like the carotid glomus, the following passage by Guild may be quoted: "The histological structure of the glomus jugulare, so far as it has been determined, is like that of the carotid body (glomus caroticum). The method of preparation used for the temporal-bone material, as has been noted above, imposes severe limitations on the study of cytologic details of the glomus

jugulare. Successful isolation of this organ in the fresh condition followed by use of special cytologic techniques may eventually reveal essential morphologic differences between it and the carotid body. As yet, however, no characteristic has been found by which, under the microscope, a section of one of these structures can be distinguished from a section of the other, when gross size and anatomic relations are disregarded" (Guild 1953, p. 1059). Nor did the study of electron microscopic cytological details show essential morphological differences between the individual tympanojugular glomera and corresponding small areas of the carotid glomus.

Vagal Glomus

7.1. Review of the Literature

7.1.1. Synonyms for the Vagal Glomus and Sub-divisions

Paragangli intravagali and paragangli iustavagali (Italian: Muratori 1932/33). Intravagale and justavagale glomusartige Gewebe (German: White 1935/36, p. 213).

Paraganglion nodosum (Latin: Watzka & Scharf 1951).

Vagal body (English: Birrell 1953/54).

Note that the term vagal paraganglion (English: Chen & Yates 1970) is not synonymous with vagal glomus, but signifies the glomus which in section 8.3 is called glomus tissue in the abdomen.

7.1.2. Site and Occurrence

Aschoff & Goodhart, in 1909, published a communication in which they mentioned that in 3 out of 80 (human) peripheral vagus nerve trunks they found accumulations of cells which according to histological structure they interpreted as sympathetic paraganglia, although no chromaffinity was observed. Muratori (1932/33), who did not quote this communication, studied the innervation of the carotid glomus in birds and a few mammals. Thereby he discovered that in relation to the vagus nerve there lay cells structurally identical with the cells of the carotid glomus. The former cells were mostly embedded in the inferior ganglion of the vagus nerve (intravagal paraganglion) or in the capsule of this ganglion (juxtavagal paraganglion). Since that time, similar results have been found in man and in an otter (de Kock 1959b), but not in the ordinary experimental animals, such as dogs and cats (de Castro 1962).

Hermann (1951) studied 300 and Stöhr (1949/50) 20 human inferior vagal ganglia using Bielschowsky silver staining. Both found paraganglionic tissue in about half the ganglia, but they do not state whether or not the tissue was chromaffin. Watzka & Scharf (1951) found five accumulations of non-chromaffin, paraganglionic tissue in or in the vicinity of one human ganglion from a 40-year-old man.

7.1.3. Light Microscopic Structure

Vagal glomera are 300–600 μm large (Watzka & Scharf 1951) accumulations situated in the connective tissue of the inferior ganglion, separated from the

ganglion cells by a connective-tissue capsule. However, White (1935/36) found the glomus cells to be in direct contact with the ganglion cells of the inferior vagal ganglion.

The glomera were made up of lobules surrounded by amply vascularized connective tissue. The predominant cell in the parenchyma was a polyhedral cell with a round or oval nucleus having a loose, net-like chromatin structure making the nucleus appear pale. The cytoplasm was delicately granular (Birrell 1953/54, Seto, Yamamoto & Fujii 1950, Watzka & Scharf 1951, White 1935/36). In addition, there were a few cells having a darker, eccentric nucleus (Birrell 1953/54, Watzka & Scharf 1951, White 1935/36). Lastly, there were mesenchymal cells, vessels, connective tissue, and mast cells (Birrell 1953/54, White 1935/36).

7.1.4. Biogenic Amines

After fixation with chromates Muratori (1932/33) found the cytoplasm of the cells in the vagal glomus to stain a light brown, a staining reaction which he described as semi-pheochromic. With a similar fixation the cells in Watzka & Scharf's (1951) human material gave no actual chromaffinity but the cytoplasm contained drop-shaped, golden granules interpreted as lipofuscin pigment.

7.1.5. Vascular Supply

The vagal glomus was supplied by a relatively large artery (Watzka & Scharf 1951), and the organ was extremely vascular, but there is not agreement on the type to which the vessels belong. Seto, Yamamoto & Fujii (1950) described them as thin veins and capillaries, Watzka & Scharf (1951) as a dense mesh-work of endothelial-lined capillaries with fairly large lumina, and Birrell (1953/54) as sinusoid vessels enclosed by endothelial cells.

7.1.6. Nerve Supply

Those workers who have studied axon-stained preparations of the vagal glomus have agreed that the glomus is very amply supplied with nerves, and that the predominant number of nerve fibres were derived from the vagus nerve. It is not known whether the nerves are afferent or efferent. Seto, Yamamoto & Fujii (1950) are the only authors who have reported finding, among extracapsular nerve fibres, apart from the moderately thick vagus fibres, also thin axons suggestive of sympathetic fibres.

When the nerves penetrated the capsule they branched extensively, but how the nerve fibres end in the organ has not been definitely elucidated. Muratori (1932/33), Seto, Yamamoto & Fujii (1950), and White (1935/36) described a complicated network of delicate fibres approximated to the parenchymal cells. According to Stöhr (1949/50) the medium-thick nerve fibres of irregular calibre

which entered the organ ended, after several divisions, as very thin fibres terminating by undulating and twisting between the cells. Birrell (1953/54) described the nerve endings as circular or club-shaped.

7.1.7. Development

Thorough embryological studies of the vagal glomus have not been performed. On the basis of serial sectioning of a small number of human fetuses Watzka & Scharf (1951) believed that the vagal glomus had the same stem cell as the cells in the peripheral parasympathetic nervous system, that the nerve fibres to the organ had their trophic centre in the inferior vagal ganglion, and that the appearance of the organ at different developmental stages was in accurate conformity with the corresponding developmental stage of the carotid glomus.

7.2. Present Investigations

The vagal glomus was sought by stepwise sectioning of one inferior vagal ganglion from each of the four fetuses. Five glomera were found, cf. Table 2.3, two from foetus cr 55 (vagal glomus cr 55a and cr 55b), two from foetus cr 59 (vagal glomus cr 59a and 59b), and one from foetus cr 62 (vagal glomus cr 62). Out of these glomera four were in a juxtavagal situation close to the surface of the ganglion (Fig. 7.1) and one in an intravagal situation inside the ganglion. In both positions the cellular clusters were in ganglionic areas predominated by nerve fibres rather than by nerve cells. Another characteristic was that the cellular clusters were lying in the mesenchyme of the ganglia. Contact between the glomus and the neighbouring axon bundles was observed in only one case (Fig. 7.3).

The accumulations were ovoid and on section about 50 μm in diameter, containing 5–15 cell nuclei. One accumulation was made up of two lobules which adhered in section planes other than that depicted in Fig. 7.3. In all cases the cellular clusters were surrounded by thin-walled vessels enveloping the cells (Figs. 7.2, 7.3, 7.4). No nerve fibres were visible in toluidine blue stained survey sections.

The nuclei in the most common type of cell were pale, of fairly irregular shape, circular or oval, diameter about 7 μm (Figs. 7.2, 7.3). The chromatin was in the central part of the nucleus in the form of small, irregularly distributed fragments, concentrated peripherally in a narrow, dense, dark rim. Nucleoli were of asymmetric situation, as a rule quite peripherally. A few cell nuclei were mitre-shaped (Fig. 7.2) or banana-shaped and somewhat denser in structure. Cells with such nuclei could tentatively be interpreted as supporting cells. Other nuclei could be identified, according to their situation, as belonging to endothelial cells or pericytes (Fig. 7.2).

The cytoplasm in the parenchymal cells was ample and the cell borders difficult to differentiate (Fig. 7.3). The cytoplasmic areas were on the whole faintly stained, but the intensity was somewhat varied, making the cytoplasm seem cloudy (Fig. 7.4). By an oil immersion lens it was possible to observe a few pale vacuoles and a few intensely staining granules.

In electron microscopic low power view (Figs. 7.5, 7.6) it was confirmed that the numerically predominant type of cell had the nuclear shape and structure observed in the light microscope. The cytoplasm of these cells contained numerous osmiophilic granules (chief cells). A few cells whose cytoplasm did not contain osmiophilic granules (supporting cells) contained nuclei of extremely irregular shape, the nuclei adapting their shape to the adjoining cells and cell processes (Figs. 7.6, 7.7, 7.8). Cytoplasmic areas which had shown a fairly homogeneous structure in the light microscope were found, on electron microscopy, to have an extremely intricate structure of cytoplasmic extensions issuing from chief cells, supporting cells, and nerve cells (Figs. 7.6, 7.7, 7.8).

At higher magnification (Fig. 7.8) it was disclosed that in the greater part of their circumference the chief cells were embraced by non-granular cell processes and in smaller areas adjoined chief-cell processes or nerve fibres (Fig. 7.18). The nerve fibres were invested through mesaxons by the supporting cells (Fig. 7.12).

The cytoplasm of the chief cells exhibited a somewhat varying electron opacity (Fig. 7.5), a difference which was not definitely due to the quantity of organelles. An organelle predominating in the juxtannuclear cytoplasm was the Golgi complex (Figs. 7.9, 7.10, 7.17), with its horseshoe-shaped stacks of cisterns, numerous small vesicles, and a few pale vacuoles. Other vacuoles (Fig. 7.9) represented vacuolated mitochondria or could not be definitely identified. Not infrequently, the Golgi zones exhibited morphological features indicating granulogenesis (Fig. 7.11).

However, specific granules did not occur especially accumulated around the Golgi zones, but were present in varying numbers throughout the cytoplasm of the chief cells. On section, the granules were found to consist of three zones (Figs. 7.16, 7.20), an electron-opaque homogeneous nucleus, a pale ring, and a vesicle. The result of measuring the diameters of the vesicles in the specific granules from each of the five vagal glomera is given in Table II. The mean of 531 granule measurements was 116 nm, standard deviation 19 nm, 95 % interval 79–154 nm.

Throughout the cytoplasm there were, in addition, rod-shaped mitochondria having transverse crests (Fig. 7.9) and in a few cases mitochondrial granules in their moderately electron-opaque matrix. Ribosomes were also present everywhere, but were not predominant. They were bound to membrane systems which occasionally formed stacks of short cisterns (Fig. 7.10), but were most often lying solitary in the cytoplasm as flat, undulating, membrane-bound cavities (Figs. 7.9, 7.16). A number of ribosomes, at an estimate as many as those

which were membrane-bound, were lying free in the cytoplasmic ground substance, sometimes in rosette-like groups (Figs. 7.9, 7.16).

In places there were centrioles, cilia of the $9 \times 2 + 0$ type (Fig. 7.17), lysosome-like bodies of different types (Fig. 7.10), adherent zonules between adjacent chief-cell plasma membranes (Figs. 7.16, 7.19), and microtubules partly scattered in the juxtannuclear cytoplasm and partly coursing parallel to the longitudinal direction of the chief-cell processes (Fig. 7.13).

At times there was a close relation between the glomus cells and the endothelial cells of the vessels (Fig. 7.15), but as a rule they were separated by a perivascular connective-tissue space containing pericytes and collagen (Figs. 7.6, 7.14). Fenestration of the endothelium occurred in both cases (Figs. 7.14, 7.15).

7.3. Discussion

Considering the size of my material, there is good conformity between the reported occurrence and site of the vagal glomus and my findings which revealed the glomus in 3 out of 4 studied ganglia, in the juxtavagal position in 4 out of the 5 cases.

The vagal glomus has not previously been studied in the electron microscope. This has confirmed what has been known in the light microscopic era, viz. that the organ is made up of vessels and nerves and a parenchyma containing two types of cell, called chief cells and supporting cells in the present description. Electron microscopy disclosed that the mutual relationship between these two types of cell may be likened to that between nerve cells and Schwann cells.

The organ is amply vascularized by thin-walled vessels having a fenestrated endothelium, and the parenchymal cells adjoin nerve fibres which in the foetus do not exhibit specializations suggesting synapses.

The organelle content of the cells has not been known previously. The content of the supporting cells exhibits no special characteristics, except that the number of organelles is fairly scanty. The chief cells contain, apart from the ubiquitous organelles, osmiophilic granules.

In my material it was not possible to distinguish the vagal glomus from a corresponding area of the carotid glomus, neither in the light microscope, electron microscope, nor by assessing the diameters of the granule vesicles (cf. Appendix II).

Stanulla & Wöckel, in their monograph (1969), state that between 50 and 60 vagal glomic tumours are on record. More recent case reports mention that the cases number only 30 (Muller & Stanisich 1970, Trail & Chambers 1970).

Thus, morphological as well as oncological studies have shown that a carotid-glomus-like tissue may be present in the inferior vagal ganglion. The histogenesis of this tissue is uncertain and its function unknown.

Glomus Tissue in Other Sites

8.1. Introduction

Section 8.2–8.11 gives a summary account of glomera which possess one or more of the following characteristics: Their relationship with the carotid glomus is not properly substantiated, their occurrence and site is inconstant, and their function is unknown.

8.2. Glomus Tissue in the Larynx

In the human larynx glomera have been reported in three different sites, here designated:

- (1) Superior laryngeal glomus. Synonyms: Glomus laryngicum superior (Latin: Kleinsasser 1966), paraganglion laryngeum (Latin: Schönberger 1967, 1969, Watzka 1966), glomus laryngicum superius (Latin: Jansen & Nettey-Marbell 1967), paraganglia laryngea superiora (Latin: Stanulla & Wöckel 1969, p. 25), superior laryngeal glomus body (English: Vettters & Toner 1970).
- (2) Inferior laryngeal glomus. Synonyms: Glomus laryngicum inferior (Latin: Kleinsasser 1964, 1966), glomus laryngicum inferius (Latin: Jansen & Nettey-Marbell 1967), paraganglia laryngea inferiora (Latin: Stanulla & Wöckel 1969, p. 25), inferior laryngeal glomus body (English: Vettters & Toner 1970).
- (3) Anterior laryngeal glomus. Synonyms: Glomus laryngicum anterior sive medium (Latin: Kleinsasser 1966), paraganglion laryngeum anterius (Latin: Stanulla & Wöckel 1969, p. 25).

Re (1). Superior laryngeal glomus.

Watzka, in 1963, published a preliminary communication on the finding of non-chromaffin paraganglia in the false vocal cord of adults. More thorough descriptions followed in 1966. Watzka's material consisted of 1 male and 1 female larynx, serially sectioned, and one of his associates (Schönberger 1966) had serially sectioned larynges from 4 neonates. Their findings were confirmed by Jansen & Nettey-Marbell (1967) who found, on serially sectioning 10 larynges from premature infants, a superior laryngeal glomus, paired in four and unpaired in one preparation. In addition, this glomus was found in the monkey and lemur, but not in the guinea-pig, dog, pig, or cat (Schönberger 1967). In the human materials the glomus was situated at the base of the false vocal cord, on a level with the upper margin of the thyroid cartilage within the anterior third of the mucosal fold. Smaller accumulations were found in relation to the

nerve fibres in the false vocal cord. The reported size of this glomus has varied: 1–1.3 mm (Schönberger 1966), 0.2–0.3 mm (Jansen & Nettey-Marbell 1967), and 0.1–0.3 mm (Watzka 1966). The organ was innervated by the internal branch of the superior laryngeal nerve.

Re (2). Inferior laryngeal glomus.

Kleinsasser reported in 1964 that in the serially sectioned larynx from a newborn infant he had found —apart from the superior glomus which he did not mention in further detail—another paired glomus, situated dorsolaterally on the cricoid cartilage. In Jansen & Nettey-Marbell's material of 10 larynges from premature infants, an organ equivalent to the inferior glomus was present in all cases. In 5 larynges it was situated, as in Kleinsasser's material, on the cricoid cartilage, whereas in the other 5 it was lying more caudally in the groove between the cricoid cartilage and the first tracheal ring. It was 0.3–0.4 mm large and was innervated by the terminal ramifications of the recurrent laryngeal nerve (Jansen & Nettey-Marbell 1967). It received a small arterial branch from the inferior laryngeal artery, and the veins drained to the venous plexuses around the larynx and oesophagus (Kleinsasser 1964).

Re (3) Anterior laryngeal glomus.

Kleinsasser (1964, 1966) found this glomus in relation to the elastic cone in a newborn infant. When measured on Kleinsasser's figures, the organ was about 0.2 mm large. Presumably, it was innervated by the external branch of the superior laryngeal nerve. A corresponding glomus was not found in the somewhat larger material of Jansen & Nettey-Marbell.

The light microscopic descriptions of the three bodies, rendered by three independent German teams, viz. Watzka & Schönberger, Kleinsasser, and Jansen & Nettey-Marbell, are identical. The bodies were invested by a capsule, the cells were arranged in clusters separated by connective tissue, and were in close relation to capillaries and in contact with nerves. Most cells were 15–18 μ m in diameter, had a pale, vacuolized cytoplasm and large, pale nuclei of a delicate, netlike chromatin structure. A few cells were smaller and contained a pyknotic-looking nucleus. In nearly all the glomera studied ganglion cells were lying in immediate relation to the glomera. According to Jansen & Nettey-Marbell (1967) the cells in the superior laryngeal glomus were non-chromaffin and non-argyrophil.

Schönberger (1969) studied the development of the superior laryngeal glomus in a material of 20 embryos and fetuses from 24–200 mm in crown-rump length. He found the parenchymal cells and the related ganglion cells to develop from parasympathicoblasts which in the smallest embryos migrated along the internal branch of the superior laryngeal nerve from the inferior ganglion of the vagus nerve. As such, the body was laid down as early as the 45 mm crown-

rump stage. The vascular labyrinth developed secondarily to the nervous elements.

Stanulla & Wöckel (1969) reported eight cases of tumours arising from the laryngeal glomus. After 1969 there has been a report of int. al. a tumour arising from the laryngeal glomus whose morphological conformity with carotid glomus tumours has been ascertained by light microscopy, electron microscopy, and study for catechol amines (Vetters & Toner 1970).

8.3. Glomus Tissue in the Abdomen

Synonyms: Abdominal vagal paraganglia (English: Goormaghtigh 1936), abdominal bodies or abdominal chemoreceptors (English: Hollinshead 1941, 1946), retroperitoneal body (English: Byrne 1958), abdominal aortic paraganglia of the "carotid" type (English: Kovrizhko 1963), retroperitoneal chemoreceptor tissue (English: Hughes 1965a), glomus-like bodies (English: Elliott 1965b), paraaortale nichtchromaffine Paraganglien (German: Stanulla & Wöckel 1969, p. 85), vagal paraganglia (English: Chen & Yates 1970).

Glomus tissue in the abdomen was found in mice by Goormaghtigh (1936), in mice and rats by Hollinshead (1941, 1946), in cats by Hughes (1965a), in hamsters by Chen & Yates (1970), and in man by Kovrizhko (1963) and Elliott (1965b). On a theoretical basis, Goormaghtigh and Elliott interpreted the finding as acetylcholine-secreting, non-chromaffin, parasympathetic paraganglia connected with the vagus nerve. Hollinshead performed nerve degeneration experiments and physiological experiments which indicated that the body was supplied by nerves having their trophic centre in the spinal ganglia and that it acted as a chemoreceptor. Kovrizhko considered it to be true chromaffin tissue, whereas Chen & Yates discussed whether it represented effector or receptor organs.

In Goormaghtigh's material of mice there were 6–20 well-defined glomic bodies distributed along the posterior vagal trunk, the posterior gastric branches, the hepatic branches in the hilus of the liver, the coeliac branches, and along the anterior vagal trunk. The largest bodies were lobulated and about $200 \times 150 \times 60 \mu\text{m}$, the smallest $60 \times 50 \times 50 \mu\text{m}$. The cells were nonchromaffin. In the large cell clusters 2–3 small ganglia were present. Chen & Yates, in electron microscopic studies of the glomus situated along the posterior vagal trunk in the hamster, found the organization of chief cells, supporting cells, and fenestrated capillaries as well as the fine structure of the cells to correspond accurately to the carotid glomera which Chen and his associates (Chen, Yates & Duncan 1969, Chen & Yates 1969) had described previously.

Hollinshead (1941)—on the basis of a material comprising more than 100 mice, 10 rats, 3 cats, 3 guinea-pigs, and 4 rabbits—reported that in the mouse there was as much glomus tissue in the abdomen as in both carotid glomera combined, but very little in the thoracic glomera. Rats had less glomus tissue

in the abdomen, but more in the thoracic glomera. In cats, rabbits, and guinea-pigs, which exhibited well-developed thoracic glomera, Hollinshead was unable to find abdominal glomera. As man has fairly well-developed aorticopulmonary glomera (making up about 1/6 of the amount of glomus tissue in the carotid glomera, cf. section 4.2.1), one would not expect to find abdominal glomera in man, if the ratio reported by Hollinshead in experimental animals between the amount of glomus tissue in the abdomen and in the chest applies universally.

However, Elliott (1965b), studying 15 human specimens consisting of the proximal 2.5 cm of the superior mesenteric artery and a piece of the anterior aortic wall immediately peripheral to the origin of the artery, found glomera in 10 of his preparations. The glomera, measuring a maximum of 0.5 mm, were situated in the median plane 1 cm from the root of the superior mesenteric artery, about 3 mm from the adventitia. In one specimen, containing the coeliac trunk, he found one glomus. According to more recent reviews (Olson & Abell 1969, Stanulla & Wöckel 1969), there have been reports on approx. 20 non-chromaffin paragangliomas assumed to have originated from the abdominal glomus tissue.

8.4. Glomus Tissue on the Base of the Heart

Synonyms: Atrial paraganglia (English: Muratori 1962b), paragangli pericoronarici (Italian: Muratori 1962a), paragangli subepicardiaci (Italian: Muratori 1964b), paraganglions épicaudiques (French: Goormaghtigh & Pannier 1939).

In man Wiesel (1906) found a body, 15 mm in length and 3–4 mm wide, made up of typical chromaffin cells, lying along the left coronary artery in the epicardiac fatty tissue medial to the left auricle. Busacchi (1912/13), in addition to the body mentioned by Wiesel, found a smaller accumulation of chromaffin cells along the right coronary artery. Along the “subpericardiac” nerves Trinci (1907) described, *int. al.* in mice, cats, pigs, and guinea-pigs, chromaffin cells whose structure was “... perfettamente simili nella struttura ai paragangli carotici” (Trinci 1907, p. 302).

Pannier (1935) as well as Goormaghtigh & Pannier (1939) reported that in the posterior atrial wall of cats there were chromaffin, non-chromaffin, and mixed paraganglia. In a rat Palme (1934) observed, superiorly in the posterior interventricular sulcus, a group of chromaffin cells and farther caudally a group of non-chromaffin cells. In a muskrat, Muratori (1959, 1962b, 1962c) found, in the cranio-posterior wall of both atria beneath the epicardium in or close to ganglia, paraganglia whose chromaffinity was inconstant. According to one of Muratori's papers (1962b) there were no atrial paraganglia in rabbits and cats, whereas according to other publications of his (1962a, 1964b, 1964c, 1969) they were indeed found. The cat which made up the material described by Muratori in 1969 had 14 approx. 40–125 μm large paraganglia in the wall of

the superior vena cava, close to its entrance into the right atrium. 8 groups of cells were highly chromaffin, 5 moderately so, and 1 contained both non-chromaffin and moderately chromaffin cells. At the entrance of the inferior vena cava there were 6 small paraganglia, 5 of which were evidently chromaffin and 1 faintly chromaffin. Beneath the epicardium on the atria, especially over the left one, and in the interatrial septum there were 18 paraganglia, 9 of which were highly chromaffin and 9 faintly chromaffin. The paraganglia were situated in relation to or were embedded in ganglia. Subepicardial glomera of approximately similar site, have been found in a seal (Blessing & Hartschen 1969), in chicks, and in pigeons (Wirtz 1968). In the terminal sulcus of the right atrium in rats, Virágh & Porte (1961) found, apart from ganglion cells, also cells which on electron microscopy showed a striking similarity to the chief cells of the carotid glomus. For this reason, the authors assumed that they were chemoreceptors.

Blessing (1963) found 9 glomera at the root of the aorta in an infant aged four weeks. Wirtz (1968) found 3 glomera at the origin of the coronary arteries in the aorta in a newborn baby. In Becker's human material (1966a, 1966b) comprising 28 large foetuses and newborns, there were 2-7, up to $100 \times 140 \mu\text{m}$ glomera per individual, situated along the course of the left coronary artery in the adventitia of the pulmonary trunk (Becker's group 1). The organization and cytological appearance of the cell clusters were identical with the findings in the carotid glomus from the same material. The cytoplasm of the chief and supporting cells exhibited neither argentaffin nor chromaffin reaction. The cytoplasm of the supporting cells was argyrophilic, unlike that of the chief cells.

In other words, it is fairly well substantiated that in man there may be glomera superoanteriorly on the base of the heart, but in man glomera have not been found farther caudally and posteriorly on the base of the heart—as has been found in experimental animals. The presence of glomera in such a position would be able to explain why glomus tumours may occur in the human posterior mediastinum (cf. Stanulla & Wöckel 1969).

8.5. Glomus Tissue in the Sympathetic Trunk

It has been reported that occasionally the right subclavian glomus in cats and rabbits may be embedded in the cervicothoracic ganglion (Muratori 1960, p. 45), and that glomera have been found in the superior cervical ganglion in a number of mammals and birds (de Kock 1959a). Detailed descriptions of glomus tissue in the superior cervical ganglion have been rendered by de Castro (1962) and de Kock (1959b).

A number of the aberrant glomera found by de Castro (1962) in dogs and cats in the vicinity of the carotid glomus were situated in the caudal pole of

the superior cervical ganglion. These glomera received their blood supply from the same source as the carotid glomus in the experimental animals concerned. Arteriovenous anastomoses were related to these glomera. By nerve degeneration experiments, it was demonstrated that the glomera were presumably innervated by the glossopharyngeal nerve.

de Kock (1959b) studied the distribution of glomus tissue on the neck of an otter. The glomera were extremely widely dispersed. After the carotid glomus, the glomus tissue embedded in the superior cervical ganglion made up the largest portion of the total glomus tissue. The size of the glomus embedded in the ganglion was $240 \times 200 \mu\text{m}$ (by way of comparison: the carotid glomus of the otter consisted of three lobes whose average size was $340 \times 200 \mu\text{m}$). The glomus was situated close to an artery, a branch of the one which furnished the carotid glomus. Studying silver-impregnated sections de Kock did not find any nervous communication between the superior cervical ganglion and the glomus, but believed that the nerve fibres followed the mentioned artery which supplied the area. In addition, smaller glomera, consisting of 10–25 cells, were detected in the wall of this artery, along the laryngopharyngeal and cardiac branches from the superior cervical ganglion and scattered in the ganglion proper.

From a developmental point of view it is interesting to note Rabl's (1922) statement that at the stage of development when the carotid glomus received fibres from the sympathetic trunk, cells were exchanged, sympathetic cells migrating to the carotid glomus and glomus cells to the sympathetic trunk.

As regards the possible occurrence of glomus tissue in the sympathetic trunk of man, it may be mentioned that Grimley & Glenner (1967) performed electron microscopic studies on three glomus tumours, one of which (Case 1) had possibly arisen from tissue in the superior cervical ganglion. This tumour, like the other two which were situated in the carotid bifurcation, contained dark-cored vesicles having a diameter of approx. 140 nm. However, this tumour had given rise to paroxysmal hypertension, and on analysis it was found to contain large quantities of pressor amines (Glenner, Crout & Roberts 1962). This finding indicates that the tumour may have been a phaeochromocytoma arising from (sympathetic) chromaffin paraganglia present in the ganglia of the sympathetic trunk. The tumour was not chromaffin, but this does not rule out a diagnosis of phaeochromocytoma (cf. Gallippi & Carrozza 1964).

8.6. Glomus Tissue in the Lungs

Synonyms: Paragangli bronchiali (Italian: Muratori 1965a) microparagangli peribronchiali (Italian: Muratori 1968), peribronchialen Mikroparaganglien (German: Böck 1970b), paraganglionäre System der Lungen (German: Stanulla & Wöckel 1969, p. 80).

On a phylogenetic and ontogenetic basis Krahle (1962) assumed that a glomus

must be attached to the 6th branchial arch artery. In accordance with this theory, it was demonstrated that the middle parts of the aorticopulmonary glomus received their vessels from the central portions of the pulmonary arteries. However, this has not been confirmed (cf. section 4.1.6). Since, however, chemoreceptor reflexes may be elicited from the pulmonary circulation (Hilpert, Schlosser, Barbey & Bartels 1964), and since a few glomus tumours have been reported in the lungs (Fawcett & Husband 1967, Stanulla & Wöckel 1969), it would seem rational to seek glomera farther peripherally along the pulmonary arteries.

Blessing & Hora (1968) serially sectioned the left lung of a newborn infant into about 5250 sections. In this material they found 68 glomera which according to size were classified into three groups: Large glomera (more than 10 glomus cells per section), which numbered 3, were lobulated glomera situated in the hilus of the lung, in the connective tissue around the main trunk of the pulmonary artery. Out of 10 medium-sized glomera (5–10 glomus cells per section) 3 were in the same position as the large ones, 3 were between the pulmonary artery and the pulmonary vein, and 4 were in the vicinity of bronchi. Out of 55 small glomera (less than 5 glomus cells per section) 5 were in the adventitia of the pulmonary artery in the hilus of the lung, 36 were scattered in the middle segments of the lung in the connective tissue of the pulmonary arteries, especially at the branchings, and 14 were in the vicinity of arteries in the connective tissue at the ramification of the bronchi in the medial parts of the pulmonary periphery. No glomera were found in the extreme periphery of the lung.

Histologically the glomera were uniform, built up of cell nests of round cells, about 15 μm large, with pale cytoplasm. The cells were separated by sinusoid capillaries and adjoined delicate nerve fibres. Close to the glomera there were often ganglion cells. The glomera were invariably situated in the proximity to a major vessel, belonging to the pulmonary artery, but whether they were in direct vascular communication with the pulmonary arteries was not apparent from the sections. Moreover, the staining method did not permit an assessment of the chromaffinity of the cells.

In a number of publications Muratori (1964c, 1965a, 1968) described intra- and extra-pulmonary glomera in relation to the trachea and bronchi of cats. The material from 1968 was described in most detail. It comprised 6 cats in which he found 24, 12, 9, 7, 3, and 3 glomera respectively, partly extrapulmonary on the anterior aspect of the tracheal bifurcation, partly intrapulmonary along the main and lobar bronchi. Out of the 58 glomera 25 were chromaffin, 25 faintly chromaffin, 2 non-chromaffin, and 3 contained chromaffin as well as non-chromaffin cells (the chromaffinity of the remaining 3 glomera is not mentioned). The glomera were supplied by vessels direct from the bronchial branches, not from the branches of the pulmonary artery. Occasionally, a direct arteriovenous anastomosis was present between the artery to the glomus and the vein from the glomus. These anastomoses were unrelated to the anastomotic

vessels containing myoepithelial cells between the branches of the pulmonary artery and the bronchial branches.

From a material of hamsters Böck (1970b) did an electron microscopic study of glomera whose situation corresponded to that found by Muratori (1968) in cats. According to Böck, the structure of these glomera—with respect to cell types, organelle content, including osmiophilic granules, nerves, synapses, and relation to vessels with fenestrated endothelium—corresponded to the appearance of other extramedullary accumulations of chromaffin cells to which Böck also assigned the carotid glomus (Böck 1970a, 1970b, Böck, Stockinger & Vyslonzil 1970).

Fröhlich (1949) also classified the so-called Feyrter cells in the bronchial mucosa (“helle-Zellen”, “clear cells”, paracrine cells, believed to be the source of carcinoid tumours of the lung) as chemoreceptors. In support of this view he stated that his own investigations had shown morphological similarity of Feyrter cells and immature taste receptor cells in the lingual mucosa and that the Feyrter cells resembled the reported descriptions of the specific cells in the carotid glomus and “glomus aorticum”. However, it must be considered more likely that the Feyrter cells make up part of a diffuse system of endocrine cells (Hage 1972), but on this basis it is not possible to rule out a relationship between glomic chief cells and Feyrter cells (cf. section 10.2.6).

8.7. Glomus Tissue in the Lower Limbs

Synonym: Femoral body (English: Burman 1956).

Assessing a number of unusual neoplasms occurring on the thigh and in the retroperitoneal tissue, and which had previously been interpreted as malignant myoblastomas, Smetana & Scott (1951) assumed that they were derived from “. . . cells composing vascular glomera of paraganglia, which are structurally similar to the carotid body and occur principally in relation to vessels traversing voluntary muscle tissue” (Smetana & Scott 1951, p. 330).

The quoted authors supported their hypothesis int. al on a communication from Johnson (1951) that “. . . there exist structures of undetermined nature, but histologically reminiscent of paraganglionic glomera, in the soft tissues surrounding the large femoral vessels . . .” (Smetana & Scott 1951, p. 558). Johnson’s bodies were in the same relation to the femoral vessels as the carotid glomus to the carotids. Tactile bodies of the Vater-Pacini type were connected with the Johnson bodies whose cells were assumed to be fairly primitive and related to epithelioid muscle cells in arteriovenous anastomoses. Since Smetana & Scott classified these tumours as non-chromaffin paragangliomas, a large number of case reports have appeared on similar tumours on the thigh and in other sites of the motor apparatus. However, the classification of the tumours is

still very much in doubt. According to Stanulla & Wöckel (1969) there is presumably a question of various types of sarcoma.

Studying osmium zinc iodide-impregnated preparations from a large animal material to elucidate the innervation of the lower-limb vessels, Lassmann & Gottlob (1970) found, between the artery and vein in the popliteal fossa of a cat, a body which they classified histologically as a non-chromaffin paraganglion.

For the purpose of deciding whether glomera exist on human lower limbs, Karnauchow (1957) performed an extremely extensive histological search of a large material comprising preparations from 5 foetuses from the third trimester, 27 infants, 2 children, and 4 adults. Out of this material the following preparations were serially sectioned: 6 preparations from infants, consisting of the medial aspect of the thigh, from the inguinal ligament to the popliteal fossa, including the adductor canal, 1 preparation from an infant consisting of the entire lateral part of the thigh muscles, from the hip to the knee, 2 preparations from a foetus consisting of the entire thigh, and 2 preparations from infants consisting of the posterior aspect of the lower limb, including the popliteal fossa. The following preparations were studied histologically in at least every third millimetre: 23 of the medial part of the thigh, 7 of the lateral part of the thigh, 1 of the posterior aspect of the thigh, 3 of the entire thigh, 3 of the contents of the adductor canal with surrounding soft tissue, 1 of the posterior portion of the leg, and 2 of the entire lower limb. Only one preparation, from an infant, exhibited a suspicious structure. On serial sectioning of this structure, compared with sections from the carotid glomus, aorticopulmonary glomus, and coccygeal glomus, it was found that it was not a glomus, but more probably a lymph node with an unusually small content of lymphoid tissue and an unusually well-developed capillary network.

8.8. Glomus Tissue in the Orbit

Synonyms: Corpuscule paraganglionnaire dans l'orbite (French: Botár & Pribék 1935), paraganglion infra-orbitaire (French: Mawas 1936), glomus ciliare or ciliary body (Latin, English: Burman 1956), paraganglion ciliare (Latin: Stanulla & Wöckel 1969, p. 26).

There are only two early, very brief reports on the normal anatomy of structures in the orbit which theoretically might be the source of orbital glomus tumours, seven of which have been recorded by Stanulla & Wöckel (1969).

Close to the ciliary ganglion of a chimpanzee Botár & Pribék (1935) found a richly vascularized and innervated body whose capsule communicated with the tunica externa of one of the posterior ciliary arteries. In this body they could distinguish two types of cell, one with large nuclei poor in chromatin and the other one with small nuclei rich in chromatin. The cells varied in shape

and size. Their cytoplasm was often vacuolized and took a pale yellow stain with chromates.

Mawas (1936), serially sectioning the orbits of a newborn infant, found a body, one mm in length, on the orbital floor beneath the orbital muscle 3–4 mm posterior to the posterior pole of the globe. The cells were epithelial and lying in clusters around vascular lumina. Mawas distinguished between small and large cells. He stated that the small ones were reminiscent of the cells in the carotid body and assumed that this orbital body was an internally secreting organ to be classified with chromaffin paraganglia.

Fisher & Hazard (1952), who published one of the first cases of orbital glomus tumours, were unable to locate a normally occurring orbital glomus in a human material of a size unstated.

8.9. Glomus Tissue Along Sensory Branches from the Mandibular Nerve

Hayek (1962), in the course of a discussion, suggested that Chievitz' juxtaoral organ might be a glomus attached to the nerve of the 1st branchial arch, the mandibular nerve. The organ of Chievitz is about 3 mm in length and 1 mm in width. It is situated posteriorly on the buccinator muscle, caudodorsally to the buccal nerve which gives off a small branch innervating the organ (Zenker 1953/54). The organ is made up of a centrally situated epithelial layer whose cells form strands and clusters or tubules filled with colloid, enveloped by a nervous layer containing numerous cells and myelinated nerves, and a thick outermost fibrous layer, built up of concentric connective-tissue lamellae (Zenker 1953/54, Zenker & Salzer 1961). The cells in the epithelial layer have developed from the epithelium of the oral cavity (Zenker 1960) and are non-chromaffin (Zenker, Mayr, Widhalm & Salzer 1961). On electron microscopic study of this organ from rats and from adult human beings the cells in the epithelial layer have proved to be of the same appearance as the cells in the epithelium of the oral cavity (Mayr & Salzer 1967, Salzer, Stockinger & Zenker 1964). I have had occasion to compare the electron microscopic appearance of the carotid glomus and of Chievitz' organ (Jensen 1970) from foetuses of almost the same age and prepared in almost the same way. Assessed on this basis and on the basis of the briefly reported, thorough investigations, there is no morphological or histogenetic basis for Hayek's assumption that the organ of Chievitz might be a glomus.

Nevertheless, there may be, as assumed by Hayek, a glomus attached to the sensory branches from the nerves of the 1st branchial arch. Whittick (1956) found a glomus tumour associated with the inferior alveolar artery and which caused pathological fracture of the mandible. Smithers & Gowing (1965) described a case of multiple glomus tumours among which the initial one, that

gave rise to symptoms, occurred on the right ramus of the mandible. Its nature as a glomus tumour was histologically confirmed at autopsy. Thus, the hypothetical glomus (alveolar body, English: Burman 1956), from which these tumours may have arisen is to be sought in the mandibular canal and must be assumed to be innervated by fibres from the inferior alveolar nerve.

8.10. Glomus Tissue in the Vicinity of the Oesophagus and Trachea

In an autopsy material Thulin (1914) described paraganglia (in the sense used by Kohn) in the adventitia of the oral part of the oesophagus, but he did not test the chromium reaction of this tissue. After the classification of paraganglia into chromaffin sympathetic and non-chromaffin parasympathetic ones, Seto (1935) uncritically grouped Thulin's finding among the latter. Watzka (1943), on the other hand, held that this was not a paraganglion at all, but no doubt "... ein verlagertes Epithelkörperchen" (Watzka 1943, p. 266). Mapping glomera in the supracardiac area, Blessing (1963) found a glomus in the oesophageal wall of a 4-week-old baby and Blessing & Hartschen (1969) one in the same site in a seal.

As mentioned in section 8.2 half the inferior laryngeal glomera in Jansen & Nettey-Marbell's material (1967) were situated below the lower margin of the cricoid cartilage and thus actually, by definition, belonged to the trachea. These authors serially sectioned the entire trachea down to the bifurcation, but found no glomera caudal to the inferior laryngeal glomus. As mentioned in section 8.6, Muratori (1968) found in the cat partially chromaffin paraganglia on the anterior aspect of the tracheal bifurcation. Glomera close to the oesophagus or trachea may possibly form the origin of paratracheal glomus tumours (Stanulla & Wöckel 1969).

8.11. Glomus Tissue Elsewhere

Synonyms: Cervico-thoracic microparaganglia (English: Muratori 1962b), corpuscule carotidiens aberrant or hétérotopique (French: de Castro 1962), ektopischen zervikalen chemorezeptorischen Zellgruppen (German: Stanulla & Wöckel 1969, p. 88).

In this section the term microglomera will be used to designate solitary glomus cells or tiny accumulations of glomus cells which are not in immediate connection with the carotid glomus or with the thoracic glomera that have received names. The localization of microglomera may be roughly collected in the following groups: (1) Cervical: In relation to the nerves to and around the carotid glomus (de Castro 1962, Meijling 1937), and embedded in the walls of the great arteries close to the carotid glomus (Meijling 1937, Nielsen 1968).

(2) Thoracic: In relation to the nerves in and around the thoracic glomera (Coleridge, Coleridge & Howe 1970, Hughes 1965a, Muratori 1962b, Nonidez 1935, 1937, Penitschka 1931), and in the walls of the great intrathoracic arteries (Blessing & Hora 1968, Nonidez 1935, 1937, Palme 1934).

In man only thoracic microglomera have been reported, whereas thoracic as well as cervical ones have been found in other mammals. In addition to the latter, birds (references in de Kock's review 1959a) have been found to have glomera in the thyroid gland, the parathyroid glands, and in the ultimobranchial bodies. If corresponding microglomera exist in man, their presence may explain the occurrence of some of the ectopic cervical glomus tumours and glomus tumours in the thyroid gland, but not the occurrence of glomus tumours in the palate, in the parotid gland, in the nose, nasal cavity, nasal sinuses, in the duodenal wall, in the bladder wall, or in the pineal body (Stanulla & Wöckel 1969).

Differential Diagnostic Investigations and Considerations

9.1. Introduction

As already mentioned, certain morphological, including fine structural, similarities have been found between glomus chief cells and chromaffin cells (cf. section 1.2.4) and between glomus chief cells and sympathetic ganglion cells (cf. section 1.2.2). Since extra-adrenal chromaffin cells and aberrant sympathetic ganglion cells may occur along the very nerves and in the very nervous plexuses to which glomus tissue is related, I studied the fine structure of sympathetic ganglion cells from the ganglia of the sympathetic trunk and of chromaffin cells from the organ of Zuckerkandl in order to avoid, as far as possible, confusing glomus chief cells with cells of these types. In connection with the report on these investigations other diagnostic possibilities will be discussed.

9.2. Differential Diagnosis from Extraadrenal Chromaffin Cells

My observations were based on electron microscopic examination of specimens from the organ of Zuckerkandl from fetuses cr 55, cr 59, cr 61, and cr 62. The specimens were prepared in the same way as the specimens containing glomera, cf. section 2.1. The specimens were less than 1/2 mm thick and were embedded in gelatin capsules.

In the light microscope (Fig. 9.1) the chromaffin tissue* was made up of densely arranged, uniform cells in strands between the vessels. The cell nuclei were round or oval, about 7 μ m large and contained 1–4 nucleoli. The cytoplasm was filled with numerous, distinct, deeply staining granules. Between the cell strands there were irregular vascular lumina, and in relation to the peripheral areas of the organ there were groups of ganglion cells and axon bundles.

In electron microscopic low power views (Fig. 9.2) the tissue gave the impression, as on light microscopy, of being uniform, predominated by one type of cell. The nuclear chromatin formed small, electron-opaque areas of delicate structure, especially in the periphery of the nuclei and around the nucleoli, leaving large areas of electron-transparent, amorphous nucleoplasm. The shape of these cells was extremely irregular, processes from one cell making their

*) For practical reasons this term will be used, although the cells do not exhibit the cytochemical staining reaction with chromium salts until the 4th-5th foetal month.

way far in between neighbouring cells. The intercellular space was of a constant width, 25–30 nm. In the cytoplasm (Fig. 9.3) the granular endoplasmic reticulum formed stacks of long, parallel cisterns or concentric, circular systems whose membranes, in both events, were studded with ribosomes. Free ribosomes also occurred, but practically only between or in the immediate vicinity of the reticular cisterns. The high-ribosome areas of the cytoplasm appeared dark in the low-power view, whereas the remaining areas of the cytoplasm in the same cell were more electron-transparent. The pale cytoplasmic areas contained the other two structures characteristic of the cells, glycogen particles and secretory granules (Fig. 9.4). The glycogen particles consisted of a basic unit of about 20 nm which with the lead stain used stood out in more marked electron density than the ribosomes. The basic unit formed rosettes of five or more particles (α -particles), but occasionally were solitary (β -particles).

A common feature of all the secretory granules within the chromaffin cells (Figs. 9.4, 9.5) was a vesicle enveloping an electron-dense material. The granules showed considerable variation in size and nuclear structure: The mean of the diameters in 782 secretory granules was calculated as 213 nm, but there was a great difference in diameter from granule to granule. This was expressed mathematically in the standard deviation (72 nm) and in the 95 % interval (71–354 nm). A numerical description of the distribution of the random samples of granular diameters from each foetus is given in Table II.

The structure of the granular cores varied from homogeneous, electron-opaque to structured, more electron transparent. There was a tendency for the structure to be denser the smaller the core. Small granules with a homogeneous, dense core and larger granules with structured core occurred in all cases in the same cell. The space between the core and the membrane of the granules usually showed an area concentric with the core. However, the core might be relatively small and asymmetric, and thus signet-ring shapes and apparently empty vesicles occurred in the ultrathin sections.

The cells also exhibited (Fig. 9.3) Golgi complex, mitochondria, agranular vesicles of a size from that of secretory granular vesicle up to half the nucleus of the cell. In a few ultra-thin sections there were centrioles and microtubules.

The vessels were made up of an extensive, fenestrated layer of endothelial cells in direct contact with the chromaffin cells. In addition to the thick bundles of axons in relation to the periphery of the organ seen in the light microscope, electron microscopy disclosed a few axons coursing between the cells.

Confusion of glomus chief cells and chromaffin cells from the material used is out of the question. A few manifest, constantly present differences will be pointed out below:

(1) The distribution of the random samples of the granular diameters in the two types of cell differed, the mean value as well as the standard deviation being greater in chromaffin cells than in glomus chief cells, cf. Appendix II and Table II.

(2) The number of granules per cytoplasmic area unit was greater in the chromaffin cells than in the glomus chief cells.

(3) The chromaffin cells contained numerous glycogen particles, an inclusion which did not (or only rarely) occur in the glomus chief cells.

(4) In the glomus chief cells the number of free ribosomes and of membrane-bound ribosomes was of the same order of magnitude, and the ribosomes were evenly distributed all over the cytoplasm. In the chromaffin cells the majority of ribosomes were membrane-bound and concentrated within delimited areas of the cells.

When the specific cells occurred in an organized form other differences also became striking:

(5) In the glomera about one-third of the parenchymal cells were agranular supporting cells, a type of cell which was extremely rare in the chromaffin tissue.

(6) The vessels in the glomera were surrounded, in large areas, by pericytes and collagen fibres which delimited the endothelium from the parenchyma. In the chromaffin tissue there was in most cases immediate contact between the parenchymal cells and the vessels whose endothelium contained a considerably larger number of fenestrae than the vessels in the glomus tissue.

(7) The number of nerve fibres coursing between the glomus cells was greater than the number of nerve fibres between the chromaffin cells.

The fine structural differentiation of chromaffin cells has been described in the rat by Elfvin (1967), in the rabbit by Coupland & Weakley (1968), and in the chick by Mastrolia & Manelli (1969). At a developmental stage corresponding to that of my foetuses, the primordium of the chromaffin tissue in these animals was predominated by a cell which Elfvin called "intermediary". It was characterized by containing two types of granules: Granules having a homogeneous core (storing noradrenaline ?) and larger granules having a structured core (storing adrenaline?). In rabbits and rats the majority of these cells also contained glycogen. At birth the extraadrenal bodies in the rabbit were predominated by cells containing granules with noradrenaline. At earlier stages of development too there were occasionally cells predominated by noradrenaline granules. As these granules are highly reminiscent, in size as well as in fine structure, of the granules in the glomera, a confusion of such chromaffin cells containing exclusively non-adrenaline granules and glomus chief cells cannot be ruled out.

9.3. Differential Diagnosis from Sympathetic Ganglion Cells

My observations were based upon the electron microscopy of preparations from the cervical sympathetic trunk ganglia of cr 61 (cf. Fig. 5.20) and cr 59

and from two foetuses of 53 and 62 mm crown-rump length. The specimens from the latter two did not meet the ideal demands of comparison mentioned in section 2.2, being from other individuals than the "corresponding" glomera (cr 55 and cr 62), and they were prepared in a different way (fixed in 5 % glutaraldehyde and embedded in Araldite, cf. Table 2.2). The specimens were less than 1/2 mm thick and were embedded in gelatin capsules.

In the light microscope (Fig. 9.6) the ganglia were found to be made up of cells, numerous axons, and a few vessels. Among the cells there were (1) cells with large nuclei paler than the cytoplasm, (2) cells with somewhat smaller nuclei slightly darker than the cytoplasm, and (3) cells with small, rather dark, usually angular nuclei. A study of the fine structure of the cells (Fig. 9.7) showed that the latter cells were satellite cells, whereas the former two had to be characterized on the basis of their organelle content as ganglion cells which at this developmental stage exhibited considerable variation in chromatin structure. The cells with loose chromatin structure were on the whole larger than those with a dense chromatin structure. The ribosomes were the all-predominant organelle in the cytoplasm (Fig. 9.8). The majority were evenly distributed in the perikaryon in the form of polyribosomes, only a small number being bound to the outside of membranes in short, flat vesicles. Nissl substance, in the form of stacks of granular endoplasmic reticulum, did not occur. The specific granules (Figs. 9.9, 9.10, 9.12) were present in small numbers in the perikarya. They were scattered in the cytoplasm, but were rather more commonly present in the cone whence the axons originated, where minor clusters might be observed. The typical granules were made up of an electron-opaque, homogeneous circular core, surrounded by a concentric electron-transparent, narrow ring, again surrounded by a vesicle made up of a unit membrane. There was but little variation in the structure and size of the granules. The mean for their diameters in 423 osmiophilic granules was 77 nm, standard deviation 11 nm, 95 % interval 54–100 nm. A numerical description of the random sample distributions of the granular diameters from each foetus is given in Table II. The Golgi complexes were juxtannuclear, the mitochondria were evenly distributed in the cytoplasm, lysosomes and centrioles were observed in a few ultra-thin sections, and neurotubules were found predominantly in the axons and in the axon hillocks.

Between the ganglion cells there were numerous axons and rather few satellite cells which encapsulated the ganglion cells but incompletely. The axoplasm in some axons was "empty", presumably due to insufficient fixation, as this phenomenon was also observed in axons in others sites, e. g. in the auricular branch of the vagus nerve. In most axons, however, there were longitudinally coursing neurotubules and small, round mitochondria. It was a characteristic finding that some of the axons contained granules of the same appearance as those described in the perikarya of the cells (Fig. 9.11).

Pick, Gerdin & Delemos (1964) described the fine structure of osmium-fixed

sympathetic ganglia from one 15-week and one 17-week-old foetus. They found membrane-bound, electron-dense inclusion bodies which were interpreted as lysosomes. According to Pick's paper read in 1966 some of these bodies were 80–120 nm large. Wechsler & Schmekel (1967), studying the fine structural differentiation of sympathicoblasts in chicks, ducks, and geese, found that at an early developmental stage the perikarya contained 50–150 nm large osmophilic membrane-bound granules. The number of granules in the perikaryon decreased with age, and the authors assumed that a somatofugal transport of catechol amine granules took place, a view which has later received experimental support (int. al. Geffen & Ostberg 1969).

Confusion of solitary glomus chief cells with sympathetic ganglion cells cannot be excluded, but the following differences between the ganglion cells in sympathetic ganglia and the chief cells of glomera may be pointed out:

(1) The distribution of granular diameters in the two types of cell differed, mean value as well as standard deviation being less in sympathetic ganglion cells than in glomus chief cells, cf. Appendix II and Table II.

(2) The number of specific granules was smaller in the ganglion cells than in the glomus chief cells. Since, however, there was a considerable variation in the number of granules per cell area in the glomera, a few glomus chief cells might contain just as few granules as sympathetic ganglion cells.

(3) The ganglion cells contained a larger number of ribosomes than the glomus chief cells. In the latter the ribosomes were fairly evenly distributed between the free and bound form, while in the latter the ribosomes were present predominantly as non-membrane-bound polyribosomes.

(4) When the two types of cell occurred in major groups, a confusion was excluded already in the light microscope because of the numerous axons of the ganglia, their few vessels and typical pale chromatin structure of their nuclei. The nuclear structure of the ganglion cells, however, varied a good deal from the classical pale ganglion-cell nuclear structure to a darker and denser structure than in the nuclei of the glomus chief cells. This factor gave rise to confusion with glomus supporting and chief cells which had dark and pale nuclei respectively, but this risk of confusion could be excluded by the aid of the electron microscope.

9.4. Differential Diagnosis from Other Granulated Cells

The cells which during the light microscopic era were considered aberrant chromaffin cells have proved, in the superior cervical ganglion of the rat, to exhibit a fine structure differing from that of chromaffin cells with endocrine secretion, especially with respect to synaptology (Matthews & Raisman 1969, Siegrist, Dolivo, Dunant, Foroglou-Kerameus, de Ribaupierre & Rouiller 1968, Williams

& Palay 1969). On this basis it is assumed that the cells are sympathetic interneurons, constituting functionally and morphologically a type of cell intermediate between endocrine secretory chromaffin cells and transmitter-secreting sympathetic neurons (Matthews & Raisman 1969). The interneurons are so reminiscent in fine structure of glomera that a confusion cannot be ruled out on the basis of the available descriptions from non-human materials. In this connection it may be mentioned that in the ganglia of the sympathetic trunk of human fetuses 49 and 77 mm in crown-rump length I have found paravascular cells whose fine structure was indistinguishable from that of the cells in the organ of Zuckerkandl (unpublished data). If these paravascular cells are the precursors of "interneurons", glomus cells cannot be confused with "interneurons" at the early foetal stage.

Like sympathetic neurons, the perikarya in the parasympathetic peripheral ganglion cells contain osmiophilic granules of the catecholamine type (Yoshida 1968). However, as the cells are reminiscent also in other ways, of sympathetic neurons, and as the number of granules is smaller, if anything, in the parasympathetic than in the sympathetic cells, a confusion ought not to take place between glomus chief cells and parasympathetic peripheral nerve cells, if these factors apply universally.

As discussed in more detail in section 10.2.5, APUD cells are endocrine cells which possess certain common fine structural features, and these features also characterized glomus chief cells. The APUD cells are localized within well-defined organs. However, this possibly does not apply to the calcitonin-producing C cells (which show fine structural APUD-cell characteristics also in embryofoetal animal material, Stoeckel & Porte 1970). The C cells develop from the pharyngeal entoderm and are localized in certain animals (e. g. in chicks and pigeons) in the ultimobranchial bodies. In other animals they are scattered in the thyroid gland, parathyroid glands, thyroglossal duct, and thymus. According to Carvalho & Pearse (1968) it may be expected, from a developmental point of view, that C cells may occur dispersed on the neck. In man, however, C cells can so far be located only in the form of parafollicular cells in the thyroid gland (Kalina, Foster, Clark & Pearse 1970). If they occur only in the thyroid gland also in the human foetus, a confusion between C cells and glomus chief cells is excluded, if only because of the site of the former.

Discussion and Conclusion

10.1. The Glomera as a System

10.1.1. Glomera as an Entity from the Morphological Point of View

As is apparent from my review of the literature, numerous workers have believed that the microscopic glomera could not be distinguished structurally from the carotid glomus. The variations in the descriptions of the individual microscopic glomera from author to author is due largely to the authors' having been influenced by their opinion of the carotid glomus, cf. section 1.2. When disregarding this influence, I have not been able to find in the literature decisive differences between the descriptions of the carotid glomus and of the individual microscopic glomera.

From my descriptions of the glomera (Sections 3–7) and the appurtenant figures (Appendix I), it is apparent that in my material it was not possible to distinguish the individual microscopic glomera from the carotid glomus. In the statistical analysis (Appendix II) of the size of the membrane-bound granules in the chief cells, it could not be excluded that the random samples from microscopic glomera and from the carotid glomera are derived from the same population.

The demands that have to be fulfilled in order to consider the glomera a well-defined, disseminated system of morphologically uniform structure are (1) that the glomera are morphologically so uniform that they are indistinguishable from each other, and (2) that the glomera may be distinguished morphologically from other types of tissue.

Re (2). The concept other types of tissue theoretically comprises an infinite number of known and unknown types of tissue. It is possible that the glomera do not differ from each of these types. However, likely possibilities of confusion may be ruled out, as demonstrated in Section 9.

Re (1). Neither in the literature, in my own light and electron microscopic studies, nor in the statistical analysis of the granule diameters have I been able to find a criterion by which the individual microscopic glomera could be distinguished from the carotid glomus. Accordingly, glomera are indistinguishable mutually. The limited differences in the morphology of the glomera are explicable by developmentally, individually, technically, or functionally conditioned differences. Thus *by the methods employed so far it has not been possible to demonstrate essential differences between glomera. Until such differences*

are demonstrated, the hypothesis that glomera belong to the same type (class) of tissue has to be maintained.

10.1.2. Glomera as an Entity from the Embryological Point of View

Onto- and phylogenetically it has been demonstrated (Boyd 1937a, Muratori 1937, 1960) that the glomera develop in relation to the branchiogenic, baroreceptive vascular zones (Palme 1944). The carotid glomus develops in relation to the 3rd branchial arch artery which persists as the cardiac segment of the internal carotid artery. The subclavian glomus develops in relation to the 4th branchial arch artery, which in man persists on the right as the root of the right subclavian artery and on the left as the aortic arch; the aorticopulmonary glomera develop in relation to the (5th-) 6th branchial arch, i. e. the bifurcation of the pulmonary trunk and the ductus arteriosus. In Boyd's (1961) opinion, however, the inferior aorticopulmonary glomus could not be assigned to this system, as it belonged rather to the common stem of the branchial arch arteries, the truncus arteriosus, than to the caudal branchial arch arteries.

It may be argued firstly that as long as it was believed that glomera were branchiogenic, derived from the mesoderm in the baroreceptive vascular zones (Boyd 1937a), an extremely intimate connection between the glomera and the respective vascular zone had to be presupposed. Later, it was discovered that the organs are branchiomic, derived from cells in the cranial nerve ganglia which migrate along the nerves corresponding to the branchial arches, i. e. along the glossopharyngeal nerve to the 3rd branchial arch and along the vagus nerve to the 4th, (5th), and 6th arch. Therefore, the final localization of the glomera will be determined more by the area of distribution of the nerve within the respective branchial arch than by the extent of the baroreceptive zone derived from the branchial arch artery. That the nervous connection of the organs predominates over their vascular connection is supported by the fact that the vessels to (at least the caudal) aorticopulmonary glomera (cf. section 4.1.6) and possibly to the carotid glomus (cf. section 3.1.6), change their site of origin in the course of development, the primary embryo-foetal vessels arising from the branchial arch arteries, whereas this does not apply to the secondary adult vessels. Moreover, the very considerable rearrangements of the three caudal branchial arch arteries in man from the embryonic to the adult vascular pattern must play a role in the localization of the structures connected with the arches.

In consequence of the branchiogenic theory Monro (1950) and Krahl (1962) have suggested that the tympanojugular glomus was the glomus of the 2nd branchial arch. Krahl claimed—in opposition to Guild (1953)—that this glomus was innervated from the nerve of the 2nd branchial arch, the facial nerve.

Furthermore, Hayek (1962) has suggested that the organ of Chievitz was the glomus of the 1st branchial arch, this organ being innervated by the buccal nerve from the nerve of the 1st branchial arch, the mandibular nerve. As stated in section 8.9 I have found no morphological or histogenetic basis for this assumption. On the other hand, it cannot be ruled out that a glomus is embedded in the corpus mandibulae (alveolar body) which might be imagined to have been laid down in relation to Meckel's cartilage. Lastly, Kleinsasser (1964) has suggested that the superior and inferior laryngeal glomera might be those of the 4th and 6th branchial arch respectively.

A marked shortcoming of the branchiogenic theory is that although it does explain the presence of the larger glomera—carotid, subclavian, aorticopulmonary—and possibly also that of a few of the smaller ones (e. g. the tympanojugular glomus), it does not explain the presence of others (e. g. the vagal glomus).

On a purely theoretical basis Dallachy & Simpson (1960) have assumed that the presence of glomera, apart from the larger ones, in higher vertebrates could be explained by the presence, throughout the musculature, of scattered, non-functioning rudiments of glomera which in lower vertebrates were segmentally laid down. Zettergren & Lindström (1951) suggested that in man the tympanojugular glomus might be a phylogenetic, non-functioning rudiment.

Actual histogenetic data are available only for the carotid glomus (section 3.1.8) and the thoracic glomera (section 5.1.8). Although it is still being discussed whether the glomus cells are mesodermal or neurogenic, the literature available to me leaves no doubt that the cells of the named glomera are derived predominantly from the ganglia connected with the glossopharyngeal nerve (carotid glomus) and the vagus nerve (subclavian glomus, aorticopulmonary glomera). This view, however, poses a new problem: In human material (van Campenhout 1948) as well as in large animal series (Batten 1960, Halley 1955, and others) it has been demonstrated that the cells in the ganglia of the sensory cranial nerves are derived from two sources: Partly from the neural crest and partly from branchial, ectodermal thickenings, so-called placodes. From which of these two sources the glomus cells are derived still remains an unsolved problem, but the following assumption will be advanced:

Re supporting cells: Considering the mesaxonic relation of these cells to the chief cells and the nerve fibres, their electron microscopic appearance (Böck, Stockinger & Vyslonzil 1970, Grimley & Glenner 1967, Hess 1968, Lever, Lewis & Boyd 1959, Ross 1959), their cytochemistry (Becker, Drukker & Meijer 1967) and their histogenesis (Rogers 1965), it must be taken for granted that like neurilemmal cells in the peripheral nervous system, they are neuroectodermal, derived from the neural crest.

Re chief cells: The structure of dedifferentiated neoplastic glomus chief cells in tumours of the vagal glomus, carotid glomus, and tympanojugular glomus has been found—by Cenci (1957), Grimley & Glenner (1967), and Balogh,

Draskóczy & Caulfield (1966) respectively—to be so similar to the cells in tumours arising from the sympathetic nervous system that in these authors' opinion the glomus tissue must have a stem cell in common with the cells of the peripheral sympathetic nervous system. If this theory is to be harmonized with the results of the histogenetic studies, it must be a presupposition that the glomus chief cells have developed from the neural crest-derived cells that take part in laying down the cranial nerve ganglia and not—as evidently presumed by the named authors—from the neuroblasts which form the chromaffin cells and ganglion cells in the sympathetic ganglia. The presumption of the relationship between sympathetic cells and glomus chief cells in the cases of Grimley & Glenner and of Balogh, Draskóczy & Caulfield was based upon the finding that on electron microscopy the glomus tumour cells showed granules of the same type as that found in normal and in neoplastic sympathetic cells. However, it is not possible to conclude direct from the granule content of the cells to their origin. Granules of a similar fine structure have been found int. al. in (mesodermal) cardiac muscle cells (Manasek 1969), in (entodermal) gustatory receptor cells (Murray & Murray 1967), and in (ectodermal) Merkel cells (Smith 1967, 1970).

Owing to the localization of non-chromaffin paragangliomas in relation to cranial nerves which carry parasympathetic fibres and to the sacral part of the parasympathetic nervous system (non-chromaffin paragangliomas on the thigh and in the abdomen) Elliott (1965a) considered the glomera to be parasympathetic analogues of the sympathetic adrenal medulla. This idea accords with the theory on non-chromaffin paraganglia which presupposes that the chief cells are homologous to the postganglionic parasympathetic neurons (cf. section 10.2.4). From a morphological point of view, however, it is highly doubtful whether glomera occur in relation to the oculomotor nerve (glomus tissue in the orbits?), facial nerve (tympanojugular glomus?), or in relation to sacral parasympathetic fibres (femoral body?).

Thus, since the presumption that the glomus chief cells have a stem cell in common with the autonomic sympathetic or parasympathetic nervous system rests upon a flimsy basis, and since more recent truly histogenetic studies of the carotid glomus have in fact disclosed that ectodermal placodal cells take part in its primordium (Batten 1960, Murillo-Ferrol 1967), or that such participation can at least not be excluded (Rogers 1965), it seems reasonable to assume that the glomus chief cells are of ectodermal derivation.

The data collected hitherto on the histogenesis and localization of the glomera in man are explicable on the basis of the following theory: The carotid glomus, subclavian glomus, and aorticopulmonary glomera are not branchiogenic (i. e. not developed from cells in the branchial arches), but branchiomic (i. e. laid down at the site of the branchial arches), developing from cells (be they neuroectodermal or ectodermal) migrating along the glossopharyngeal nerve and vagus nerve to the 3rd, 4th, (5th), and 6th branchial arch where they organize

under the influence of and in the vicinity of the branchiogenic baroreceptive vascular zones. The other glomera are aberrant in the sense that they have arisen from cells which have been erroneously retained (e. g. the vagal glomus) along their normal route of migration or have lost their way, proceeding along the branches of the glossopharyngeal and vagus nerves (e. g. the tympanojugular glomus).

10.1.3. Glomera as an Entity from the Functional Point of View

Physiologists are of the opinion that the glomera, together with the baroreceptive vascular zones, constitute the receptor link in the afferent part of reflex arcs which—by their influence upon the central nervous system centres for ventilation and circulation—take part in the maintenance of an oxygen and blood supply sufficient for the organism as a whole (Gernandt 1946, Heymans & Neil 1958, Witzleb 1970).

On the basis of the branchiogenic theory Krah1 (1962) believed that the glomera were involved in the regulation of the blood supply to structures which had developed from the respective branchial arches, the "glomus pulmonale" for instance being the glomus of the 6th branchial arch artery, connected with the regulation of the pulmonary circulation. Gosses (1936) suggested that the glomera were "on guard" for organs which were particularly sensitive to changes in the composition of the blood, the glomus tissue in the orbit for instance protecting the retina, the tympanojugular glomus the middle ear (Bartels 1949), the laryngeal glomera the larynx (Kleinsasser 1966), glomera in the vicinity of ganglia protecting the latter from oxygen deficiency (Hughes 1965a, 1965b), and the aorticopulmonary glomera securing adequate circulation through the coronary circulation (Knoche & Schmitt 1963).

However attractive such theories may seem, it must be borne in mind that chemoreceptor function has been demonstrated only in the carotid glomus and in the thoracic glomera, i. e. in the branchiomic glomera, whereas the presumption of function in the aberrant glomera is based exclusively upon their morphological similarity with the carotid glomus. (An exception is formed by the abdominal glomera in mice and rats from which Hollinshead (1941, 1946) elicited chemoreceptor reflexes by non-adequate stimuli).

In my opinion, however, the demonstration of specific chemoreceptive function need not necessarily be a condition for classifying a glomus as being of the same tissue type as the carotid glomus. The differentiation of the embryonic and competent glomus chief cells derived from the cranial nerve ganglia might be imagined to require induction from the branchiogenic baroreceptive vascular zones corresponding to the cranial nerves, possibly by way of the primary vessels developed from these vascular zones. This role of the primary vessels

might explain the strange fact that they extend very far in the retrograde direction along the nerves along which the glomus cells migrate (Hammond 1941) and that when their induction has been completed the vessels may undergo retrogression, giving place to secondary vascular supply apparently determined exclusively by the organs having to be supplied with blood from the nearest artery carrying oxygenated blood. The cells in the aberrant glomera have not always been exposed to such an induction needed for function. However, as the cells do not differ histogenetically—and thereby morphologically or with respect to oncogenic potentials—from the cells in the organs subjected to induction, they must still be interpreted as glomus chief cells.

10.1.4. Glomera as an Entity from the Oncological Point of View

The interpretation of the glomera as a system is lastly based upon the fact that outside the carotid bifurcation there may occur tumours histopathologically similar to carotid glomus tumours (Appel 1959, Burman 1956, Byrne 1958, Evans 1968, Le Compte 1951, Stanulla & Wöckel 1969). This view has been supported especially by the finding that glomus tumours in different sites in the same patient may occur as primary, synchronous, or asynchronous, multicentric neoplasms (Dallachy & Simpson 1960, Lattes 1950, Lattes, McDonald & Sproul 1954, Stanulla & Wöckel 1969, Wilson 1970, Wychulis & Beahrs 1965, Zacks 1958). This is the basis which has bred thoughts underlying titles such as “The chemoreceptor system and its tumor—the chemodectoma” (Burman 1956, p. 330).

In assessing these tumours, however, several factors urge to caution: (1) Differential diagnostic possibilities are numerous and the histological diagnosis difficult. Stanulla & Wöckel (1969) adduced int. al. the following possibilities of histopathological errors: Haemangioendothelioma, anaplastic carcinoma, adenoma, granular cell tumour (= granular cell “myoblastoma”), alveolar soft-tissue sarcoma (= malignant organoid granular cell “myoblastoma”), glomangioma, and tumours arising from the sympathetic nervous system (ganglionic neuroma, neuroblastoma, ganglionic neuroblastoma, benign and malignant phaeochromocytoma) (2) There are some unexplained nosological differences between tumours arising from the different glomera with respect to bilaterality, sex ratio, familial occurrence, radiosensitivity, and degree of malignancy (Boyd, Lever & Griffith 1959, Rauch 1969). (3) When multicentric tumours are present it is difficult to decide whether they represent several primary tumours or one primary with metastases (Dallachy & Simpson 1960, Lattes, MacDonald & Sproul 1954, Zacks 1958).

Thus, the occurrence of a glomus tumour does not justify the deduction that a glomus occurs normally at the site of the tumour concerned.

10.2. Attempts at Classifying Glomera

10.2.1. *The Essential Element*

The interpretation of the glomera as a system of anatomically separate, uniform structures, is thus based not only upon morphological, normal anatomical, but also upon onto- and phylogenetic, physiological, and oncological findings. How to classify this system of uniform structures and what to call it is problematic, since as yet there has never been agreement concerning a classification of the carotid glomus, cf. section 1.2. With a view to attempts at classification, a few comments will be devoted to which element of the thoroughly studied carotid glomus is most probably the essential one.

It might be imagined that the nerve endings in the carotid glomus were directly sensitive to adequate stimuli. de Castro (1944, 1951) and Zapata, Hess & Eyzaguirre (1969) have re-innervated the carotid glomus by connecting the peripheral stump of the severed sinus nerve to sensory branches from the vagus nerve. After a suitable period of growth they could record chemoreceptor activity in the new-formed nerves. These experiments definitely exclude that the fibres of the sinus nerve make up the specific chemoreceptive element of the organ. Of course, there is a theoretical possibility that the carotid glomus was merely re-innervated by specific chemoreceptive vagus fibres from the thoracic glomera or from the glomus tissue in the larynx. However, this does not appear likely, and therefore it must be assumed that the glomus cells (1) induce specific chemoreceptive function in the nerve endings, (2) that the glomus cells are chemoreceptors which, presumably by a chemical transmitter mechanism (Eyzaguirre, Koyano & Taylor 1965, Eyzaguirre & Zapata 1968) transmit their messages to "non-specific" nerve endings. However, Böck, Stockinger & Vyslonzil (1970), the only workers who have found nervous mitochondrial sacs in the carotid glomus, assumed that these nerve terminals, not the glomus cells, were the chemoreceptive element of the organ.

de Kock and Dunn (de Kock 1954, de Kock & Dunn 1964, 1966) are among the few who have doubted that of the two types of parenchymal cell in the carotid glomus the chief cells are the chemoreceptive element. This was because they demonstrated that the chief cells were not in direct contact with vessels and nerves. The neurovascular contact of the cells was part of the structural basis for de Castro's chemoreceptor hypothesis which presupposed that the epithelioid cells in the carotid glomus had a "pôle sanguin" in contact with the vascular endothelium and a "pôle nerveux" (de Castro 1951, p. 14) in synaptic contact with the afferent fibres of the sinus nerve. de Kock's and Dunn's studies revealed that the chief cells were entirely separated from the vascular endothelium by supporting cells and that a large part of the nerve fibres in the carotid glomus ended in mesaxons in the supporting cells without attaining contact with the chief cells. In brief, these authors demonstrated that the supporting cells, rather than the chief cells, fulfilled the demand of a "ner-

vous pole" and a "vascular pole" and that, therefore, the supporting cells were more probably directly involved in chemoreception.

To de Kock's and Dunn's view it may be objected, in the first place, that the supporting cells resemble neurilemmal cells (cf. section 10.1.2). Secondly, the oxygen consumption in the carotid glomus is of the same order of magnitude as that in the brain (Fay 1970), and carbonic anhydrase (Becker, Drukker & Meijer 1967, Woods 1967) has been demonstrated in the chief cells in such appreciable quantities that the enzyme must be assumed to play a role in the turnover rate of carbon dioxide and hydrogen ions. Thus, despite the presence of the supporting cells, the chief cells may be in close "contact" with changes in the gas composition of the blood. Thirdly, the fact that a number of nerves possibly end in the supporting cells need not mean that these cells are the specific chemoreceptors. If chief cells and nerve fibres are invested in the supporting cells through the same mesaxons, transmitter substance given off by the chief cells will be able to diffuse to the nerve fibres through the intermembranous space formed by the mesaxons. This latter theory presupposes that the chief cells transmit their messages to afferent nerves chemically, i. e. that they produce, and upon adequate stimuli give off, a transmitter substance. Although the chemical nature of such a substance is not known, it very probably exists (Eyzaguirre, Koyano & Taylor 1965, Eyzaguirre & Zapata 1968).

It is reasonable to believe that the specific granules in the chief cells represent a transmitter reservoir which upon adequate stimuli is given off by the chief cells. In severe hypercapnia (75 % CO_2 for 1–4 minutes) Blümcke, Niedorf & Rode (1967) demonstrated intracytoplasmic rupture of the vesicles of the specific granules which emptied out the osmiophilic core substance into the cytoplasm. Upon severe, short-lasting hypoxia Blümcke, Rode & Niedorf (1967) observed a movement of the granules towards the plasma membrane and exocytotic emptying of the granular content. Such an effect was not demonstrable in moderate hypoxia lasting from minutes to hours (Al-Lami & Murray 1968a, Blümcke, Rode & Niedorf 1967, Chen, Yates & Duncan 1969, Zapata, Hess, Bliss & Eyzaguirre 1969). Release of granules, thus, is not observed until at a degree of anoxia which *per se* is fatal and which in general has a marked effect upon the fine structure of cells. On this basis it cannot be concluded that the granules release their content upon physiological variations in the oxygen tension.

In assessing the reported hypoxia experiments, however, the following factors must be taken into consideration: (1) The electron microscopic picture obtained when the animals are killed after the exposure to hypoxia is a "snapshot" of a dynamic process which comprises release of granules and newformation of granules. In mild degrees of hypoxia the newformation can keep up with the release, and the number of granules remains constant. In moderately severe short-lasting hypoxia (9 % O_2 for 45 minutes) newformation may possibly over-compensate for the release, so that the number of granules increases (Al-

Lami & Murray 1968a). In moderately severe, long-lasting hypoxia (5 % O_2 for 3 hours) atypical granules form, showing a bean-shaped core or a double core (Zapata, Hess, Bliss & Eyzaguirre 1969). In severe, short-lasting hypoxia (2.5 % O_2 for 5–10 minutes) the release of granules exceeds what the Golgi complex can synthesize, and the number of granules decreases (Blümcke, Rode & Niedorf 1967). (2) As with other peripheral transmitter reservoirs (Iversen 1967), it must be imagined that a possible transmitter in the chief cell occurs in different pools which with varying ease are given off from depots to the cytoplasm and/or from the cytoplasm to the extracellular space. If the specific granules represent a relatively stationary form of depot, the number of granules cannot be expected to fall until the cells have been exposed to long-lasting and marked stimulation. (3) On reserpine stimulation of the carotid glomus it has been demonstrated, by fluorescence microscopy and electron microscopy (Niedorf, Rode & Blümcke 1970), that practically the entire catechol amine content of the chief cells could be released without this giving rise to demonstrable fine structural changes in the organ. In other words, as might be expected, appreciable biochemical changes may take place without being reflected in the fine structure. (4) Although it was demonstrated that upon adequate stimulation the chief cells give off the content of their granules, it cannot be directly deduced that the extracellular effect of the released substance is nerve stimulation or that the extracellularly active substance is a catechol amine (cf. section 10.2.4).

From the physiological point of view it is assumed that a disturbance of energy mechanisms in the glomus chief cells, induced by the adequate stimuli, causes the release of a transmitter which activates centripetal nerves (Joels & Neil 1968). The chemical nature of the sensory transmitter has not been elucidated (Torrance 1968). Although a structural basis for this experimentally supported assumption has not been found, the morphologists operate with the concept "a functional unit" (Becker 1966a, Becker, Drukker & Meijer 1967, Fería-Velasco, González-Angulo & Zavala 1966, Grimley & Glenner 1968) consisting of one or more chemoreceptive chief cells with appurtenant (afferent and efferent) nerves, invested in one (or more) supporting cells.

Incidentally, different functional roles have been attributed to the glomus chief cells: (1) The chief cells are specific receptor cells whose sensitivity to adequate stimuli is controlled by efferent nerves; on stimulation exceeding the threshold value a neurotransmitter is given off (Becker, Drukker & Meijer 1967, Grimley & Glenner 1968). (2) The chief cells are specific receptor cells which upon adequate stimulation give off a neurotransmitter which activates afferent nerves as well as a hormone (Blümcke, Rode & Niedorf 1967, Morita, Chiocchio & Tramezzani 1970). (3) The chief cells are cells with efferent innervation which upon stimulation from the nerves give off a transmitter which acts upon (modulates) the sensitivity of specifically chemoreceptive nerve endings to the adequate stimuli (Biscoe, Lall & Sampson 1970). (4) The chief cells are

endocrine cells with efferent innervation whose function is independent of specifically chemoreceptive nerve endings (Böck, Stockinger & Vyslonzil 1970).

Although, from a morphological point of view, the last-mentioned possibility cannot be ruled out, I feel it must be justified to consider the glomus chief cells as an element so essential to the chemoreceptive function that attempts at classifying organs made up of this type of cell should be based upon the characteristics of these cells, since these cells condition the functional, structural, and patho-anatomical characteristics of the organ. The other elements—i. e. the nerves, supporting cells, vessels, and connective tissue—are no doubt necessary to function, but they do not differ fundamentally from corresponding elements of other organs.

10.2.2. Glomus Chief Cells as Myoepithelioid Cells

Assessment of the specific cells in chemoreceptive glomera and in vascular glomera discloses that it is only in preparations stained by the conventional histological staining methods (Schumacher 1938) that the cells of the two organs look alike. More special histochemical studies of the cells in the carotid glomus and in the coccygeal glomus have revealed marked differences (Hollinshead 1942). On electron microscopy of a biopsy containing a digital glomus from a youngish man with no circulatory disturbance, Martines, Tischendorf, Curri & Manzoli (1965) found the epithelioid cells to show interdigitating plasma membranes with desmosomes; the predominant cytoplasmic structure was myofibrils. The most striking cytoplasmic structure in the glomus chief cells is the specific granules. A similar difference exists between the fine structure of the cells in a glomangioma on a finger (Murad, Haam & Murthy 1968) and carotid glomus tumours (Grimley & Glenner 1967).

Since, thus, there are essential differences between the specific cells in the two types of organ, I feel it must be out of the question to classify glomera as arteriovenous anastomotic organs, even though arteriovenous shunts may be present in the glomera (de Castro 1940, 1951, Goormaghtigh & Pannier 1939).

10.2.3. Glomus Chief Cells as Modified Ganglion Cells

Such a classification might be supported on (1) the glomus chief cells being provided with processes which contain microtubules of the same size as neurotubules, (2) the chief cells containing granules resembling those of neurons in the central nervous system and in the peripheral nervous system (Bloom & Aghajanian 1968, Geffen & Ostberg 1969), and (3) the chief cells, like ganglion cells, being surrounded by neurilemmal cells.

On the other hand, none of these characteristics is specific of ganglion cells: (1)

Microtubules occur in all cells during mitotic division and exist in many cells as a cytoskeleton in the interphase, (2) specific granules of the same structure as in the above-mentioned neuro-ectodermal cells are present also in non-neuroectodermal cells (cf. section 10.1.2), and (3) satellite cells (supporting cells) occur around the receptive cells in the sensory epithelium of the gustatory, auditory, vestibular, and olfactory organs (Wyburn 1960).

10.2.4. Glomus Chief Cells as Paraganglionic Cells

A classification of glomera as paraganglia must depend upon how the concept paraganglion is defined. It was originally introduced by Kohn (1900) as a term for the adrenal medulla and homologous structures. The criteria which must be demanded for assigning a tissue to this class are (1) that the cells are homologous to the postganglionic sympathetic ganglion cells, (2) that their main innervation is sympathetic efferent nerve fibres, homologous to the preganglionic sympathetic fibres, (3) that the cells are endocrine, catechol amine-secreting, and (4) that the cells are chromaffin. These criteria are not fulfilled by the glomera.

Watzka (1930/31) introduced the term non-chromaffin paraganglia for a parasympathetic homologue of the chromaffin paraganglia. The criteria which must be demanded for assigning a tissue to this class are (1) that the cells are homologous to the postganglionic parasympathetic ganglion cells, (2) that their main innervation is parasympathetic efferent nerve fibres, homologous to the preganglionic parasympathetic fibres, (3) that the cells are endocrine, secreting an acetylcholine-like substance, and (4) that the cells are non-chromaffin. These criteria are not fulfilled by the glomera.

The concept sensory paraganglion, described by Goormaghtigh & Pannier (1939), is somewhat vague, but departs radically from the original definition of paraganglia, the authors presupposing that the cells were receptive and that their main innervation was afferent: "L'appareil récepteur est une cellule nerveuse spéciale d'allure glandulaire (cellule p. g.) capable d'analyser les variations chimiques du sang. Influencée par ces dernières, la cellule paraganglionnaire libère une substance qui stimule à son tour les terminaisons des nerfs sensitifs" (Goormaghtigh & Pannier 1939, p. 510). Although Goormaghtigh & Pannier's theory still applies with respect to glomic function, their classification of the organs as paraganglia rests upon an extremely flimsy basis, since—like Watzka (1943) who extended the concept paraganglion to comprise "... "neurogene Nebenorgane" ... im Bereiche des peripherischen Nervensystems" (Watzka 1943, p. 262)—they presupposed that the cells had developed from the neural crest for which there is no decisive proof, as already stated in section 10.1.2.

A classification of glomera as endocrine catechol amine-secreting cells of a type like phaeochromocytes cannot be based upon the osmiophilic granules and catecholamine content of the chief cells: Neurosecretory cells in the supraoptic and paraventricular nuclei of the hypothalamus contain osmiophilic granules

(Bargmann & Gaudecker 1969); the hormones which these cells give off are low-molecular polypeptides, vasopressin, and oxytocin. Endocrine APUD cells (cf. section 10.2.6) contain osmiophilic granules as well as catechol amines. The secretion given off by these cells is low-molecular polypeptides; the role of the biogenic amines in APUD cells is unknown (Håkanson 1970). Osmiophilic granules in catechol amine-neurotransmitter secreting sympathetic axon terminals (Geffen, Livett & Ruch 1969) and in endocrine, catechol amine-secreting adrenal medullary cells (Helle & Serck-Hanssen 1969) contain both catechol amines and proteins. Thus, it cannot be concluded from the morphology or catechol amine content of the granules whether a cell is an endocrine secreting or a transmitter-secreting cell or whether the secreted, extracellularly active substance is a polypeptide or a catechol amine.

10.2.5. Glomus Chief Cells as Gustatory Receptor Cells

Costero (1963) reported that in the laboratory where he worked the carotid glomus had been found to be of the same histological appearance as the taste buds. On this basis he characterized the carotid glomus as an endosensory organ "... the taste organ of the blood" (Costero 1963, p. 270). However, Costero's starting point, the structural similarity of glomus chief cells and the cells of the taste buds, can only partially withstand a fine structural evaluation. The cells in the taste buds exhibit marked polarity (Murray & Murray 1967). Apically, the plasma membranes are interdigitating and furnished with desmosomes and microvilli. The apical cytoplasm in dark cells contains granules which resemble int. al. the granules of glomus chief cells: "These granules are enclosed in a membrane and resemble neurosecretory and "catechol-amine granules" seen in other tissues" (de Lorenzo 1963, p. 11).

10.2.6. Glomus Chief Cells as APUD Cells

On the basis of a series of investigations, summarized in a review from 1969, Pearse defined a series of cells, the so-called APUD cells which have the common feature of forming, storing, and giving off hormones characterized chemically as low-molecular polypeptides. There is a question of the following cells (hormone added in brackets): Cells in the adenohypophysis (adrenocorticotrophin and melanotrophin), beta-cells (insulin), alpha-1-cells (gastrin), and alpha-2-cells (glucagon) in Langerhans islets in the pancreas; thyroid and extrathyroid C cells (calcitonin); argyrophil cells (gastrin), and argentaffin cells (gastrin, secretin) in the stomach; argyrophil cells (cholecystokinin, pancreazymine), and argentaffin cells (secretin, glucagon) in the intestine. In addition possibly the cells of the adrenal medulla (medullarin?), Feyrter cells in the lungs (pneumo-

kinin?), glomus chief cells (glomins?), pinealocytes in the pineal body (Carvalho, Welsch & Pearse 1968).

The definition of the APUD cells is based upon certain common fine structural and cytochemical features, the latter being considered of most importance. The abbreviation APUD is derived from the initials of the Anglo-Saxon words which designate the most important cytochemical characteristics of the cells: "amine and amine-precursor uptake and decarboxylation" (Pearse 1969, p. 306). Glomus chief cells have the following features in common with APUD cells:

(1) The chief cells exhibit the fine structural features, i. e. slight content of granular endoplasmic reticulum, a large content of agranular vesicles, many free ribosomes, fixation-labile mitochondria, and membrane-bound granules of a size ranging from 100 to 200 nm.

(2) The chief cells contain fluorogenic biogenic amines, noradrenaline, dopamine, and 5-hydroxytryptamine (Becker, Drukker & Meijer 1967, Blümcke, Rode & Niedorf 1967, Dearnaley, Fillenz & Woods 1968, Muratori, Chiarini & Battaglia 1966, Niedorf, Rode & Blümcke 1970, Hamberger, Ritzén & Wersäll 1966).

(3) The chief cells take up catechol amine- and indol amine precursors (amino acids). Autoradiography has revealed uptake of (^3H) 3,4-dihydroxyphenylalanine and (^3H) 5-hydroxytryptophan (Chen & Yates 1969, Gershon & Ross 1966, Helpap & Hempel 1968). Pre-treatment with 3,4,5-trihydroxyphenylalanine increased the number of specific granules in the carotid glomus by 50 % (Hellström 1971).

(4) The chief cells contain alpha-glycerophosphate dehydrogenase (Fine, Enriquez & Morales 1968).

(5) The carotid glomus from experimental animals as well as man contains cholinesterase and/or non-specific esterase (Becker, Drukker & Meijer 1967, Fine, Enriquez & Morales 1968, Palkama 1965, Pryse-Davies, Dawson & Westbury 1964, Ross 1957b, Serafini-Fracassini & Frasson 1966). The esterases are localized int. al. in the cytoplasm of the chief cells, but as there has been no histochemical-electron microscopic study, it is not known in what part of the cells the activity is localized. In APUD cells there is esterase activity in relation to the nuclear membrane, plasma membrane, Golgi membrane, and the membranes of the endoplasmic reticulum.

The final decision as to whether the glomus chief cells can be characterized as APUD cells depends upon whether they contain a characteristic polypeptide. A hint concerning this question may be had by studying masked metachromasia (Solcia, Vassallo & Capella 1968) which discloses proteins with a high content of side-chain carboxyl groups. The final criterion, however, is whether immunofluorescence demonstrates the presence of a specific low-molecular polypeptide in the cells.

10.2.7. Glomus Chief Cells as Specific Receptor Cells

The above attempts at classifying glomus chief cells indicate certain morphological similarities with endocrine cells (APUD), with neurons, and with gustatory receptor cells. On the other hand, each of these characteristics emphasizes only part of the features which characterize the glomus chief cells. It is reasonable, therefore, to classify the cells as a separate type. This type of cell makes up the essential element in organs whose primary function is specific chemoreception (cf. sections 10.2.1 and 1.2.6). Oorgans made up of the cell type in question should accordingly be classified as specific receptor organs, a view which has been sharply formulated by Le Compte: "... the carotid body, together with the similar cardio-aortic bodies, should be classified as a specialized chemoreceptor and not as a gland of internal secretion, paraganglion, or arteriovenous glomus" (Le Compte 1948, p. 308).

Nonidez (1937) characterized glomera as: "... complex neurovascular structures intimately associated with the branchial arches of the embryo" (Nonidez 1937, p. 311). The past three decades' research has not been able to do away with this claim, glomera being consistently characterized from the anatomical point of view as follows: (1) Specific chief cells invested in supporting cells, (2) afferent innervation, (3) specialized, ample vascular supply, (4) embryological association with the branchiogenic, baroreceptive vascular zones or with the afferent nerves to these zones, the glossopharyngeal and vagus nerves.

10.3. Suggested Terms for the Glomera

10.3.1. Restriction of the Number of Names

In order not to increase the existing confusion of the nomenclature in this field, I shall disregard the possibility of introducing new designations or adopt terms such as ganglion, gangliolum, glomerulus, gland, and nodule which have never gained much ground. The terms most commonly used to-day for organs made up of glomus tissue are restricted to corpus or body, glomus, non-chromaffin paraganglion, and for tumours originating from glomus tissue to carotid body like tumours, non-chromaffin paragangliomas, and chemodectomas.

10.3.2. Glomus and Corpus

The Latin word glomus in fact stands for a rolled-up body, a ball. The word is used in descriptive histology to indicate a nest of cells and small vessels, cf. the diminutive form renal glomerulus. In this sense it was originally used in *Nomina anatomica* (1895) for the carotid glomus as well as the coccygeal glomus. Regrettably, the term glomus coccygeum has been replaced by corpus

coccygeum in the last edition of *Nomina anatomica* (1968). The same prefix, has been given to the aorticopulmonary glomera, which are called corpora para-aortica; the glomus caroticum has retained its former prefix. In order to find a way out of the unfortunate custom of using the same term for organs of entirely different tissue types, such as the corpus coccygeum (= glomus coccygeum) and corpora paraaortica (= glomera aorticopulmonalia) and of using different terms for organs made up of the same tissue type, such as the glomus caroticum and corpora paraaortica, the vascular glomera should retain their original name glomus and the chemoreceptive glomera—in consequence of a historical misunderstanding, cf. sections 1.2.7 and 10.2.2—should be re-named e. g. corpus.

10.3.3. Non-chromaffin Paraganglion

Regardless of the sense in which the term paraganglion is used (cf. section 10.2.4) the term is unfortunate, as it implies that the cells are neuroectodermal, and where the glomera are concerned this is doubtful. The addition non-chromaffin is also a doubtful characteristic, as the cells presumably stain with chromium salts, though faintly (cf. section 3.1.5). And this term is a complete misnomer when applied to glomus tumours, as true paragangliomas (phaeochromocytomas) may be non-chromaffin (Gallippi & Carrozza 1964). The use of the term paraganglion should be restricted to organs which are made up of phaeochromocytes.

10.3.4. Chemodecton

If it is desired to stress in the nomenclature that the chemoreceptive glomera are made up of a tissue differing in type from vascular-arteriovenous and chromaffin tissues, a non-characterizing term, such as corpus, would be appropriate. But if we accept the claim that "there is now no doubt that namesmanship has hindered the analysis of published knowledge quite seriously..." (Elliott 1965a, p. 1818), a more characterizing designation has to be selected.

Since de Castro's pioneer studies from 1926 and 1928 physiologists have called the glomera chemoreceptors. However, this hybrid is not suitable as a name, as it is used in a wide sense for all organs which are able to record chemical substances, i. e. also for the organs of taste and smell (e. g. de Lorenzo 1963, Wyburn 1960). Mulligan (1950) introduced the term chemodectoma (dechethai = to receive) for glomus tumours. This term has ever since been used to a considerable extent in clinical and pathological publications (Appel 1959, Burman 1956, Stanulla & Wöckel 1969, Wychulis & Beahrs 1965, Zacks 1958), and it is preferred in the World Health Organizations's international histological classification of tumours (Enzinger 1969). Grimley & Glenner (1967) have objected to this term that it is doubtful whether the tumours function. Since, how-

ever, there is no doubt about the fundamental function of the normal organs, the name might be applied to them. If we add to the root chemodect- the Greek suffix -on, signifying "entity" we have the name chemodecton.

The individual glomera could be named according to their localization. The branchiomeric glomera it would seem natural to name after the vascular segment with which they are associated during embryonic life, e. g. carotid chemodecton, subclavian chemodecton, and aorticopulmonary chemodecta. The aberrant glomera, which judging by all appearances belong to the same morphological tissue entity, would then, from a systematic point of view, be named after the nerves to which they are related, e. g. chemodecton of the auricular branch of the vagus nerve (chemodecton ad ramum auricularem n. vagi) and chemodecton of the tympanic branch of the glossopharyngeal nerve (chemodecton ad nervum tympanicum n. glossopharyngei). From a practical point of view a simpler localizing term would be appropriate, e. g. tympanojugular chemodecton (chemodecton tympanojugulare) and vagal chemodecton (chemodecton vagale).

One of the approved principles of the International Anatomical Nomenclature Committee is that "... no attempt would be made to provide an official name for every minute structure that has ever been discovered and described" (*Nomina anatomica* 1968, p. 62). The carotid glomus and the aorticopulmonary glomera are already adopted on the list of names in the *Nomina anatomica*. According to the principle mentioned, the subclavian glomus and the aberrant glomera definitely do not deserve official names. There is a possibility that the subclavian glomus might be assigned to the aorticopulmonary glomera, and the other glomera could then be collected under the term aberrant chemodecta (chemodecta aberrantes). Thus, the chemodecton system (systema chemodectum) in man would comprise the carotid chemodecton (chemodecton caroticum), the aorticopulmonary chemodecta (chemodecta aorticopulmonalia), and aberrant chemodecta (chemodecta aberrantes).

Summary

11.1. Introduction

The present investigation was a comparative study of human glomus tissue. Glomus tissue is taken to comprise the carotid glomus and structures described as having the same morphology or function as the carotid glomus or believed to have the capacity to develop tumours which are histopathologically indistinguishable from tumours originating from the carotid glomus. The work was based upon a study of the localization and structure of the glomus bodies, and its chief aim was to elucidate whether there are, outside the carotid bifurcation, glomera which may be classified morphologically as being identical with the carotid glomus. The most thoroughly studied structure, the carotid glomus, has been classified as a modified autonomic ganglion, an endocrine gland of entodermal derivation, a sympathetic chromaffin paraganglion, a parasympathetic non-chromaffin paraganglion, a sensory paraganglion, and as a myoepithelioid arteriovenous anastomosis of mesodermal derivation.

11.2. Present Investigations. Material and Technique

The present investigations comprise electron microscopy of the carotid glomus, the aorticopulmonary glomera, the left subclavian glomus, the right subclavian glomus, the tympanojugular glomus, and the vagal glomus. The glomera were sought by stepwise sectioning of epoxy resin-embedded preparations from 4 human foetuses, crown-rump lengths 55, 59, 61, and 62 mm. The material was fixed in glutaraldehyde and post-fixed in osmium. The survey sections were stained with toluidine blue, the ultrathin sections stained with zinc uranyl and lead.

11.3. Carotid Glomus

Review of the literature: The carotid glomus is situated medially in the carotid bifurcation. It measures approx. $3.3 \times 2.2 \times 1.7$ mm. It is lobulated, and the amount of connective tissue decreases with advancing age. According to recent light and electron microscopic studies there is no doubt that the principal elements are the chief cells (epithelioid cells), supporting cells, vessels with pericytes, and nerve fibres with neurilemma. Histochemically it has been demon-

strated that the chief cells contain catechol amines and 5-hydroxytryptamine. The cells are non- or semi-chromaffin. The vessels which supply the carotid glomus arise from the carotids close to their bifurcation. In the course of development they possibly change their site of origin. Arteriovenous anastomoses form in the connective-tissue capsule of the organ; each lobule is supplied by its own arteriole. The main arteries and the arteriovenous anastomoses have baroreceptive innervation. The main innervation to the parenchymal cells is made up of sensory fibres from the glossopharyngeal nerve which is in synaptic contact with the chief cells. Histogenetically it has been demonstrated that the greater part of the cellular material is derived from the ganglia of the glossopharyngeal nerve, but it still remains unelucidated whether the cells are ectodermal (from epibranchial microplacodes) or neuroectodermal (from the neural crest). The author advances the hypothesis that the chief cells are ectodermal and the supporting cells neuroectodermal.

Present findings: In the light microscope the cells form strands and whorls around the vessels. In the electron microscope the parenchyma is made up of chief cells characterized by containing membrane-bound, osmiophilic granules 110 nm in mean diameter. The cells are almost completely invested by supporting cells. It is assumed that chief cells and nerve fibres are embedded in the supporting cells through the same mesaxons. In my foetal material the glomus cells exhibited all the fine structural features described in previous materials of adults. In the foetus there is no specialized synaptic contact between nerve terminals and chief cells, no myelination of the nerve fibres, and there are no basal laminae around the vessels or glomus cells.

11.4. Aorticopulmonary Glomera

Review of the literature: The aorticopulmonary glomera are made up of a varying number of partially coherent accumulations of cells, situated within a lambda-shaped figure extending like a cord of varying thickness parallel to the concave under aspect of the aortic arch above the right pulmonary artery from the left coronary artery to the entrance of the ductus arteriosus of the attachment of the ligamentum arteriosum to the aorta. Hence a process extends down posterior to the right pulmonary artery on the right of the ductus arteriosus (ligamentum arteriosum) into the bifurcation of the pulmonary trunk. This glomus divides, often into three parts, a superior one situated immediately below the highest point of the aortic arch, a middle one in relation to the bifurcation of the pulmonary artery, and an inferior one between the pulmonary trunk and the ascending aorta. With advancing age the glomerular lobules become separated by connective tissue, so that the glomus tissue presents itself as up to fifty separate islets. The lobules are made up of large polygonal cells which are non- or semi-chromaffin. The nerves are predominantly vagus fibres having

their trophic centre in the sensory ganglia of the vagus nerve. Postnatally, the vessels arise from the arch of the aorta, the ascending aorta, or the coronary arteries. Antenatally the vessels to the caudal glomera arise from the pulmonary trunk. The arteries form arteriovenous anastomoses and have baroreceptive innervation. The chief cells are derived from the ganglia of the vagus nerve.

Present findings: Within the area where they might be expected according to the literature, 14 aorticopulmonary glomera were found. None of them could be distinguished from the carotid glomus on light microscopy of survey sections or on electron microscopy of ultra-thin sections.

11.5. Subclavian Glomus

Review of the literature: In experimental animals the right subclavian glomus is situated in relation to the root of the right subclavian artery. A corresponding glomus is rarely present in man and has been demonstrated only in embryo-foetal materials. The left subclavian glomus is situated, in experimental animals, at the root of the left subclavian artery or on the sinistro-ventral surface of the aortic arch. A corresponding glomus is seldom found in human foetuses, and if so most often in relation to the left vagus nerve where it crosses the sinistro-ventral surface of the aortic arch. In animals the organs are in time disintegrated by connective tissue. The cell clusters are built up of epithelioid cells and smaller, spindle-shaped cells. The majority of the cells are non-chrom-affin. The vessels to the cell clusters arise from the subclavian arteries, the brachiocephalic trunk, or the arch of the aorta. Each lobule is supplied by its own arteriole. The main innervation of the organs is from the vagus nerve and has its trophic centre in the sensory ganglia of this nerve. The cells of the glomerular parenchyma have developed from vagus-derived, neuroblast-like cells.

Present findings: Within the area of the left subclavian glomus the present studies disclosed seven glomera five of which were situated caudally on the sinistro-ventral surface of the aortic arch. The other two glomera found on the left side, plus one glomus found on the right side, were situated in relation to thin, vertically coursing nerves. None of these glomera could be distinguished by its fine structure from the carotid glomus.

11.6. Tympanojugular Glomus

Review of the literature: Along the course of the auricular branch of the vagus nerve and the tympanic branch of the glossopharyngeal nerve, in relation to the superior bulb of the jugular vein or in the middle ear, there are per temporale bone an average of 2.82 glomera about $500 \times 200 \mu\text{m}$ in diameter. The

cells are nonchromaffin. The nerve fibres to these organs are believed to be derived from the named nerves. The vessels arise from the inferior tympanic artery from the ascending pharyngeal artery. Cells resembling parasympathicoblasts occur along the tympanic nerve from the 125 mm crown-rump stage.

Present findings: Along the course of the tympanic branch of the glossopharyngeal nerve, from the inferior ganglion to the promontory, three glomera were found, and in the adventitia of the superior jugular bulb there were five glomera two of which were in immediate relation to the auricular branch of the vagus nerve. The cell clusters could not be distinguished by their fine structure from the cell clusters in the carotid glomus.

11.7. Vagal Glomus

Review of the literature: One or more glomera occur in or in the vicinity of about half of all human inferior vagal ganglia. The glomus tissue is amply vascularized and innervated from the vagus nerve. The parenchyma is made up of large, pale, polyhedral non-chromaffin cells.

Present findings: Five glomera were found, four of which were in an intravagal position and one in a juxtavagal position in relation to the inferior vagal ganglion. The cell clusters could not be distinguished by their fine structure from the carotid glomus.

11.8. Glomus Tissue in Other Sites

Review of the literature: Glomus tissue has been described in sites other than those mentioned above, but the relationship of these bodies to the carotid glomus is not so well substantiated. Moreover, their occurrence and sites are inconstant. There is a question of glomus tissue in the larynx (in the false vocal cord, dorsolaterally on the cricoid cartilage and in relation to the elastic cone), glomus tissue along the abdominal course of the vagus nerve, at the base of the heart, in the cervical part of the sympathetic trunk, in the lungs, in relation to the femoral and popliteal vessels, in the orbits, in relation to sensory branches of the mandibular nerve, in relation to the oesophagus and trachea. Besides, there may be cervical and thoracic microglomera in relation to nerves and vessels around the carotid glomus and the named thoracic glomera.

11.9. Differential Diagnostic Investigations and Considerations

Since mistaking glomus chief cells for chromaffin cells or for sympathetic ganglion cells could not be excluded on the basis of reported data on the fine

structure of the two last-mentioned types of cell, I performed electron microscopy of a foetal material. The chromaffin cells proved so different from glomus chief cells that a confusion is out of the question, whereas a possibility of confusing certain atypical glomus chief cells' and sympathetic ganglion cells cannot be ruled out.

11.10. Conclusion

The present investigations have demonstrated that the aorticopulmonary glomera, the right and left subclavian glomus, the vagal glomus, and the tympanojugular glomus—judging by the fine structure of their cells, statistical analysis of the size of their specific granules, the mutual relation of the cells, and their relation to vessels and nerves—are indistinguishable from the carotid glomus in human foetuses aged 10–11 weeks. The literature also does not yield any criterion by which the individual glomera can be distinguished from the carotid glomus.

The localization of the glomera in man may be explained histogenetically by the derivation of the glomera from cells in the sensory ganglia of the vagus nerve and glossopharyngeal nerve. The cells organize in the vicinity of the branchiogenic, baroreceptive vascular zones or occur in an aberrant situation along the named cranial nerves or their branches.

The glomus chief cells condition the structural, functional and patho-anatomical characteristics of the glomera. Tissue made up of this type of cell differs morphologically from other known tissue types (autonomic ganglia, paraganglia, vascular glomera, gustatory receptors, endocrine glands). It is suggested, therefore, that glomera be classified as a separate type of organ. This type is characterized in being made up of specific chief cells with afferent innervation and specialized vascularization and in being related embryologically to the branchiogenic baroreceptive vascular zones or to the nerves supplying these zones, viz. the glossopharyngeal and vagus nerves.

On this basis, the author feels it must be justified to interpret the glomera as a disseminated occurrence of the same type of tissue. The term chemodecton is suggested for structures made up of this tissue type.

Resumé

(Summary in Danish)

11.1. Indledning

Nærværende arbejde er en sammenlignende undersøgelse af humant glomusvæv. Glomus omfatter glomus caroticum og strukturer, der er blevet beskrevet som havende samme morfologi eller funktion som glomus caroticum eller er blevet tillagt evnen til at udvikle tumorer, som histopatologisk ikke kan skelnes fra tumorer udgået fra glomus caroticum. Arbejdets grundlag er en undersøgelse af glomusforekomsters lokalisation og struktur, og dets hovedsigte er at belyse, om de uden for karotisbifurkaturen liggende glomera i morfologisk henseende kan klassificeres som værende identiske med glomus caroticum. Det grundigst undersøgte af organerne, glomus caroticum, har været klassificeret som et modificeret autonomt ganglie, en endodermalt derivede endokrin kirtel, et sympatisk kromaffint paraganglie, et parasympatisk non-kromaffint paraganglie, et sensitivt paraganglie og som en mesodermalt derivede myoepiteloid arteriovenøs anastomose.

11.2. Egne undersøgelser. Materiale og teknik

Egne undersøgelser omfatter elektronmikroskopi af glomus caroticum, glomera aorticopulmonalia, glomus subclavium sin., glomus subclavium dx., glomus tympanojugulare og glomus vagale. Glomera er fundet ved trinskæring af epoxy-resinindlejrede præparater fra fire humane fetus crown-rump længder 55, 59, 61 og 62 mm. Materialet er fikseret i glutaraldehyd og efterfikseret i osmium. Oversigtssnittene er farvet med toluidinblåt, ultrasnittene kontrasteret med zinkuranyl og bly.

11.3. Glomus caroticum

Litteraturgennemgang: Glomus caroticum ligger mediallyt i karotisbifurkaturen. Det er ca. $3,3 \times 2,2 \times 1,7$ mm stort. Det er lobuleret, og bindevævsmængden tiltager med alderen. På grundlag af nyere lys- og elektronmikroskopiske undersøgelser er der ingen tvivl om, at hovedelementerne udgøres af hovedceller (epiteloide celler), støtteceller, kar med pericyter og nervetråde med neurilemma. Histokemisk er det påvist, at hovedcellerne indeholder katekolamin og 5-

hydroxytryptamin; cellerne er non- eller semi-kromaffine. Karrene til glomus caroticum afgår fra karotiderne nær deres bifurkatur; under udviklingen skifter karrene muligvis afgangssted. I organets bindevævskapsel dannes arteriovenøse anastomoser; hver lobulus forsynes af sin egen arteriole. Hovedarterierne og de arteriovenøse anastomoser er baroreceptivt innerveret. Hovedinnervationen til parenkymets celler udgøres af sensitive tråde fra n. glossopharyngeus, der er i synaptisk kontakt med hovedcellerne. Histogenetisk er det påvist, at størstedelen af cellematerialet stammer fra n. glossopharyngeus' ganglier, men det er endnu ikke klarlagt, om cellerne er ektodermale (fra epibrankiale mikroplacoder) eller neuroektodermale (fra crista neuralis). Den hypotese, at hovedcellerne er ektodermale og støttecellerne neuroektodermale, fremsættes.

Egne undersøgelser: Lysmikroskopisk danner cellerne strøg og hvirvler omkring karrene. Elektronmikroskopisk er parenkymet opbygget af hovedceller, der karakteriseres ved at indeholde membranbegrænsede, osmiofile granula med en middeldiameter på 110 nm. Cellerne er næsten helt indkapslet af støtteceller. Det antages, at hovedceller og nervetråde er indlejret i støttecellerne gennem de samme mesaxoner. Glomuscellerne i mit fetale materiale udviser alle de tidligere i adulte materialer beskrevne finstrukturelle træk. Hos fetus findes ikke specialiseret synaptisk kontakt mellem nerveterminaler og hovedceller, ingen myelinering af nervetrådene og ingen basallaminae omkring kar og glomusceller.

11.4. Glomera aorticopulmonalia

Litteraturgennemgang: Glomera aorticopulmonalia udgøres af et vekslende antal delvis sammenhængende celleansamlinger, beliggende inden for en lambda-formet figur, der strækker sig som en streng af vekslende tykkelse parallelt med den konkave underside af aortabuen over a.pulmonalis dx. fra a.coronaria sin. til ductus arteriosus' indmunding respektive ligamentum arteriosum's tilhæftning til aorta med en herfra afgående udløber ned bag a.pulmonalis dx., til højre for ductus arteriosus (ligamentum arteriosum) ind i bifurcatio trunci pulmonalis. Dette glomus deles i tre dele, en øverste beliggende umiddelbart under det højeste punkt i aortabuen, en midterste i relation til pulmonalisbifurkaturen og en nederste mellem truncus pulmonalis og aorta ascendens. Med alderen spredes glomuslobuli af bindevæv, så glomusvævet forekommer som op mod et halvt hundrede adskilte øer. Lobuli er opbygget af store polygonale celler, der er non- eller semi-kromaffine. Nerverne er overvejende vagustråde med trofisk centrum i n.vagus' sensitive ganglier. Karrene afgår postnalt fra arcus aortae, aorta ascendens eller aa. coronariae; prænalt afgår karrene til de kaudale glomera fra truncus pulmonalis. Arterierne danner arteriovenøse anastomoser og er baroreceptivt innerveret. Hovedcellerne stammer udviklingsmæssigt fra n.vagus' ganglier.

Egne undersøgelser: Inden for det efter litteraturen forventede område fandtes 14 aortikopulmonale glomera. Hvert af disse kunne ikke ved lysmikroskopi af semitynde snit eller ved elektronmikroskopi af ultratynde snit skelnes fra snit fra *glomus caroticum*.

11.5. *Glomus subclavium*

Litteraturgennemgang: *Glomus subclavium* dx. ligger hos forsøgsdyr i relation til roden af *a.subclavia* dx. Et tilsvarende *glomus* findes kun sjældent hos mennesket og er kun påvist i embryofetale materialer. *Glomus subclavium* sin. ligger hos forsøgsdyr ved roden af *a.subclavia* sin. eller på *arcus aortae*'s sinistro-ventrale flade. Et tilsvarende *glomus* findes hos humane fetus kun sjældent og da hyppigst i relation til *n.vagus* sin., hvor denne krydser den sinistroventrale flade af *arcus aortae*. Hos dyr desintegreres organerne med alderen af bindevæv. Cellehobene er opbygget af epiteloide celler og mindre tenformede celler. Flertallet af cellerne er non-kromaffine. Karrene til cellehobene afgår fra *aa.subclaviae*, *truncus brachiocephalicus* eller *arcus aortae*; hver lobulus forsynes af sin egen arteriole. Organernes hovedinnervation stammer fra *n.vagus* og har trofisk centrum i denne nerves sensitive ganglier. *Glomusparenkymets* celler er udviklet fra *vagus*deriverede neuroblastlignende celler.

Egne undersøgelser: Inden for venstre *glomus subclavium* område fandtes syv glomera, hvoraf fem lå kaudalt på *arcus aortae*'s sinistroventrale flade. Herudover fandtes to glomera på venstre side og ét på højre, der var karakteriseret ved at ligge i relation til tynde vertikalt forløbende nerver. Ingen af de pågældende glomera kunne på finstrukturen skelnes fra *glomus caroticum*.

11.6. *Glomus tympanojugulare*

Litteraturgennemgang: Fordelt langs forløbet af *ramus auricularis n.vagi* og *n.tympanicus n.glossopharyngei* i relation til *bulbus v.jugularis sup.* eller i mellemøret ligger pr. høreknogle gennemsnitlig 2,82 glomera, hvis størrelse er ca. $500 \times 200 \mu\text{m}$. Cellerne er non-kromaffine. Nervetrådene til organerne menes at stamme fra de ovennævnte nerver. Karrene afgår fra *a.tympanica inf.* fra *a.pharyngea ascendens*. Parasympatikoblastlignende celler optræder langs *n.tympanicus* fra 125 mm crown-rump længde stadiet.

Egne undersøgelser: Langs *n.tympanicus n.glossopharyngei*'s forløb fra ganglion inf. til promontoriet fandtes tre glomera, og i adventitia af *bulbus v.jugularis sup.* fandtes fem glomera, hvoraf to lå i umiddelbar relation til *ramus auricularis n.vagi*. Cellehobene kunne på finstrukturen ikke skelnes fra cellehobene i *glomus caroticum*.

11.7. Glomus vagale

Litteraturgennemgang: Ét eller flere glomera forekommer i eller i nærheden af ca. halvdelen af humane ganglia inf. n.vagi. Glomusvævet er rigeligt vaskulariseret og innerveret fra n.vagus. Parenkymet er opbygget af store lyse polyhydrale non-kromaffine celler.

Egne undersøgelser: Der fandtes fem glomera, hvoraf fire lå i en intravagal position og ét i en jukstavagal position i relation til ganglion inf. n.vagi. Cellehobene kunne ikke på deres finstruktur skelnes fra glomus caroticum.

11.8. Glomusvæv i andre lokalisationer

Litteraturgennemgang: Glomusvæv er beskrevet i andre lokalisationer end de ovennævnte, men disse forekomsters slægtskab med glomus caroticum er mindre veldokumenteret, og deres forekomst og lokalisation er inkonstant. Det drejer sig om glomusvæv i strubehovedet (i plica vestibularis, dorsolateralt på cartilago cricoidea og i relation til conus elasticus), glomusvæv langs det abdominale forløb af n.vagus, på basis cordis, i truncus sympathicus' cervicale del, i lungerne, i relation til femoral- og poplitealkarrene, i orbita, i relation til sensitive grene fra n.mandibularis, i relation til esophagus og trachea samt cervikale og torakale microglomera i relation til nerver og kar omkring glomus caroticum og de navngivne torakale glomera.

11.9. Differentialdiagnostiske undersøgelser og overvejelser

Da mulighed for forveksling af glomushovedcellerne med kromaffine celler og med sympatiske ganglieceller ikke kan udelukkes på grundlag af de foreliggende litteraturoplysninger om de to sidstnævntes finstruktur, har jeg elektronmikroskopet dem fra et fetalt materiale. De kromaffine celler viste sig herved at være så forskellige fra glomushovedceller, at forveksling er udelukket, medens mulighed for forveksling mellem enkelte atypiske glomushovedceller og sympatiske ganglieceller ikke kan udelukkes.

11.10. Konklusion

Min undersøgelse har vist, at glomera aorticopulmonalia, glomus subclavium dx. et sin., glomus vagale og glomus tympanojugulare bedømt på finstrukturen af cellerne, statistisk analyse af størrelsen af de specifikke granula, cellernes indbyrdes relation og relation til kar og nerver ikke kan skelnes fra glomus caroticum hos 10–11 uger gamle humane fetus. Ej heller ved gennemgang af litte-

raturen findes et kriterium, på hvilket de enkelte glomera kan skelnes fra glomus caroticum.

Glomera's lokalisation hos mennesket kan histogenetisk forklares ved, at glomera stammer fra celler i n.vagus' og n.glossopharyngeus' sensitive ganglier. Cellerne organiserer sig i nærheden af de brankiogene baroreceptive karzoner eller er aberrant beliggende langs de pågældende hjernenerver eller deres grene.

Glomushovedcellerne betinger organernes strukturelle, funktionelle og patologisk-anatomiske særkende. Væv opbygget af denne celletype adskiller sig morfologisk fra andre kendte vævstyper (autonome ganglier, paraganglier, vaskulære glomera, gustatoriske receptorer, endokrine kirtler), hvorfor det foreslås, at glomera klassificeres som en selvstændig organtype. Denne karakteriseres ved at være opbygget af specifikke hovedceller med afferent innervation og specialiseret karforsyning og ved at have embryologisk tilknytning til de brankiogene baroreceptive karzoner eller de til disse zoner førende nerver, n.glossopharyngeus og n.vagus.

På dette grundlag mener jeg det berettiget at opfatte glomera som en dissemineret forekomst af én og samme morfologisk veldefinerbare, selvstændige vævstype. Strukturer opbygget af denne vævstype foreslås benævnt chemodecton.

Micrographs

For marking on the micrographs the following abbreviations are used among others:

aer	agranular endoplasmic reticulum	mg	mitochondrial granule
cc	chief cell	mpv	micropinocytotic vesicle
ce	centriole	mt	microtubule
cf	collagen fibres	mx	mesaxon
ch	chromatin	ne	nuclear envelope
ci	cilium	nf	nerve fibre
cm	plasmalemma	nl	nucleolus
ct	connective tissue	np	nuclear pore
d	desmosome-like	nt	neurotubule
db	electron-dense body	nu	nucleus
en	endothelium	pc	pericyte
ep	endothelial pore	pcc	chief cell process
fb	fibroblast	psc	supporting cell process
g	Golgi apparatus	r	ribosome
gc	ganglion cell	rbc	red blood cell
ger	granular endoplasmic reticulum	sc	supporting cell
gl	glycogen	sg	specific granule
is	intercellular space	sw	Schwann cell
lb	lysosome-like body	va	vacuole
lu	lumen	vcb	vesicle-containing body
m	mitochondrion	ve	vessel
		vs	vesicle

The micrographs are grouped as follows:

Carotid glomus Figs. 3.1–3.22	Right subclavian glomus Figs. 5.20–5.32
Inferior aorticopulmonary glomus Figs. 4.1–4.17	Tympanojugular glomus Figs. 6.1–6.40
Middle aorticopulmonary glomus Figs. 4.18–4.29	Vagal glomus Figs. 7.1–7.20
Superior aorticopulmonary glomus Figs. 4.30–4.45	Organ of Zuckerkandl Figs. 9.1–9.5
Left subclavian glomus Figs. 5.1–5.19	Sympathetic trunk ganglia Figs. 9.6–9.12

The individual glomera are illustrated in the following figures:

Carotid glomus cr 55.

Figs. 3.3, 3.7, 3.13, 3.14, 3.15, 3.16

Inferior aorticopulmonary glomus cr 55.

Figs. 4.1, 4.2, 4.4, 4.5, 4.6, 4.14, 4.17

Middle aorticopulmonary glomus cr 55.

Fig. 4.27

Superior aorticopulmonary glomus cr 55.

Figs. 4.34, 4.36, 4.37, 4.39, 4.44

Left subclavian glomus cr 55.

Figs. 5.8, 5.18

Tympanojugular glomus cr 55.

Figs. 6.2, 6.3, 6.19, 6.30

Vagal glomus cr 55a.

Figs. 7.4, 7.18, 7.19

Vagal glomus cr 55b.

Figs. 7.5, 7.10, 7.12, 7.13, 7.15

Carotid glomus cr 59.

Figs. 3.2, 3.4, 3.8, 3.9, 3.10, 3.11, 3.21

Inferior aorticopulmonary glomus cr 59.

Figs. 4.8, 4.15

Middle aorticopulmonary glomus cr 59.

Figs. 4.18, 4.19, 4.21, 4.22, 4.23, 4.24, 4.26

Superior aorticopulmonary glomus cr 59.

Figs. 4.30, 4.32, 4.35, 4.38, 4.41, 4.42

Left subclavian glomus cr 59a.

Figs. 5.4, 5.17

Left subclavian glomus cr 59b.

Figs. 5.12, 5.13, 5.19

Tympanojugular glomus cr 59.

Figs. 6.16, 6.17, 6.20, 6.27, 6.33, 6.34, 6.38, 6.39

Vagal glomus cr 59a.

Figs. 7.6, 7.8, 7.9, 7.16, 7.17

Vagal glomus cr 59b.

Figs. 7.3, 7.11, 7.14

Carotid glomus cr 61.

Figs. 3.5, 3.12

Inferior aorticopulmonary glomus cr 61a.

Figs. 4.3, 4.9, 4.10, 4.12, 4.16

Inferior aorticopulmonary glomus cr 61b.

Fig. 4.13

Middle aorticopulmonary glomus cr 61a.

Figs. 4.20, 4.25

Middle aorticopulmonary glomus cr 61b.

Fig. 4.29

Superior aorticopulmonary glomus cr 61.

Figs. 4.33, 4.40, 4.43

Left subclavian glomus cr 61.

Figs. 5.9, 5.10

Carotid glomus cr 62.

Figs. 3.6, 3.17, 3.18, 3.19, 3.20, 3.22

Inferior aorticopulmonary glomus cr 62.

Figs. 4.7, 4.11

Middle aorticopulmonary glomus cr 62.

Fig. 4.28

Superior aorticopulmonary glomus cr 62.

Figs. 4.31, 4.45

Left subclavian glomus cr 62a.

Fig. 5.6

Left subclavian glomus cr 62b.

Figs. 5.5, 5.7, 5.15, 5.16

Left subclavian glomus cr 62c.

Figs. 5.2, 5.3, 5.11, 5.14

Right subclavian glomus cr 62.

Figs. 5.21–5.32

Tympanojugular glomus cr 62a.

Figs. 6.4, 6.5, 6.25, 6.26, 6.40

Tympanojugular glomus cr 62b.

Figs. 6.6, 6.7

Tympanojugular glomus cr 62c.

Figs. 6.8, 6.9, 6.18, 6.31, 6.32, 6.36, 6.37

Tympanojugular glomus cr 62d.

Figs. 6.10, 6.11, 6.28, 6.29

Tympanojugular glomus cr 62e.

Figs. 6.12, 6.13, 6.21, 6.22

Tympanojugular glomus cr 62f.

Figs. 6.14, 6.15, 6.23, 6.24, 6.35

Vagal glomus cr 62.

Figs. 7.1, 7.2, 7.7, 7.20

Fig. 3.1.

Preparation of carotid bifurcation. Carotid glomus cr 55.

The preparation was embedded in the flat end of a Beem capsule, oriented so that the vessels were cut longitudinally. The photograph was taken by transillumination of the Maraglas-imbibed specimen before polymerization of the resin.

Magnification: $\times$ ca. 35.

1. Carotid glomus.
2. Common carotid artery.
3. Internal carotid artery.
4. External carotid artery.
5. Sinus nerve.

Fig. 3.2.

Light microscopic low power view of a longitudinal section through the carotid bifurcation. Carotid glomus cr 59.

Carotid glomus (3) lying in immature mesenchymal connective tissue between the internal carotid artery (5) and the external carotid artery (6). In the connective tissue around the carotid glomus, at its upper pole, the sinus nerve (1), nerve fibre bundles in the intercarotid plexus (1), and thin-walled vessels (2), at its lower pole the artery to the glomus (4). The framed area is shown in higher magnification in Fig. 3.4.

Magnification: $\times$ 110.

1. Sinus nerve and parts of the intercarotid plexus.
the intercarotid plexus.
2. Venous vessels around the upper pole.
3. Carotid glomus.
4. Glomus artery.
5. Internal carotid artery.
6. External carotid artery.

Figs. 3.3, 3.4, 3.5, and 3.6.

Light microscopic photomicrographs of the carotid glomera cr 55, cr 59, cr 61, and cr 62.

Numerous chief cells (2) with round, pale nuclei, often with nucleoli. A few cells may probably be identified as supporting cells (1), others as pericytes (3). The glomus cells are arranged in dense strands around the vessels (4). Between the cellular areas loose connective tissue (5).

Magnification: $\times$ 640.

1. Supporting cells.
2. Chief cells.
3. Pericytes.
4. Vessels.
5. Mesenchyme.

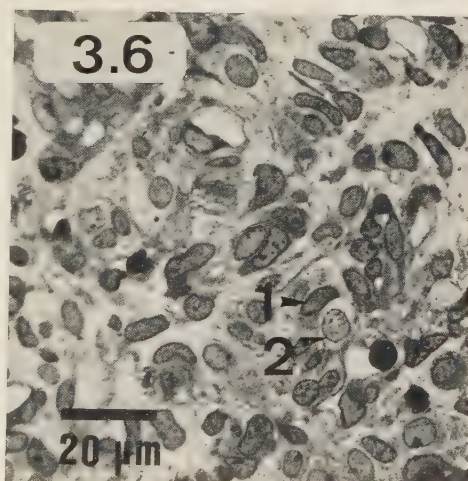
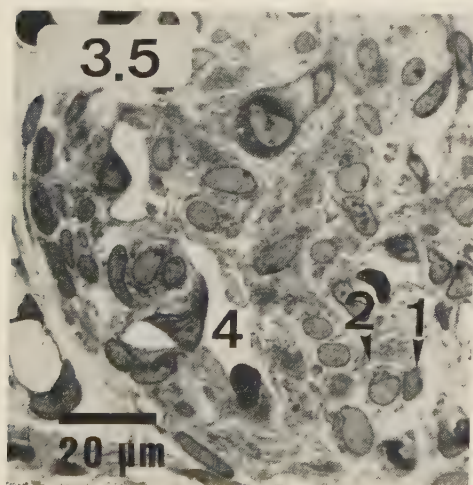
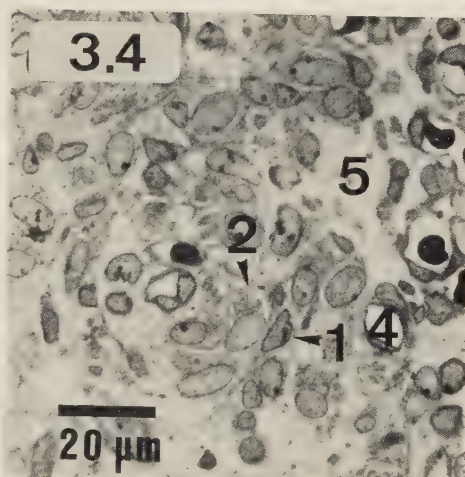
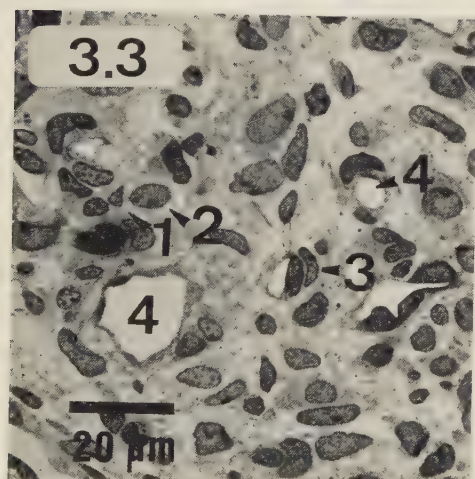
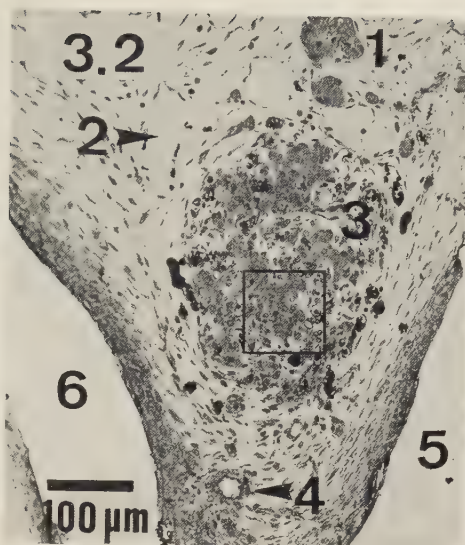
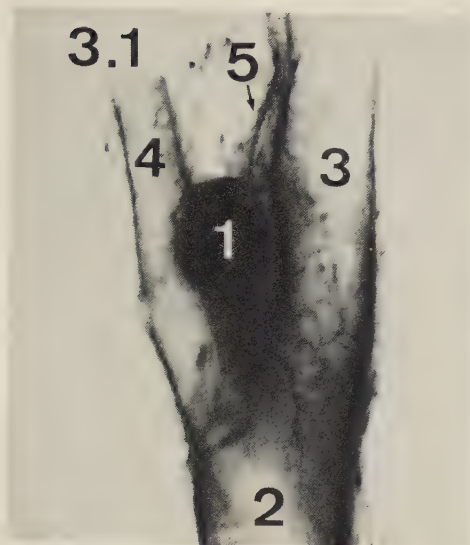


Fig. 3.7.

Electron microscopic low power view. Carotid glomus cr 55.

This picture illustrates the general histological architecture of the glomus with vessels (ve), pericytes (pc), chief cells (cc), longitudinally and transversely cut processes from the chief cells (asterisks), supporting cells (sc) with processes (arrows) as well as bundles of nerve fibres (nf) interposed between the cells. The cytoplasm of the chief cells shows electron opacity in even transitions (cc₃) from pale (cc₂) to dark (cc₁). The nuclei of the chief cells contain nucleoli (nl), and their cytoplasm is rich in organelles. Outstanding features are varying quantities of punctate, dark granules, mitochondria of varying size and shape, and pale vacuoles.

Magnification: $\times 4,200$.

3.7

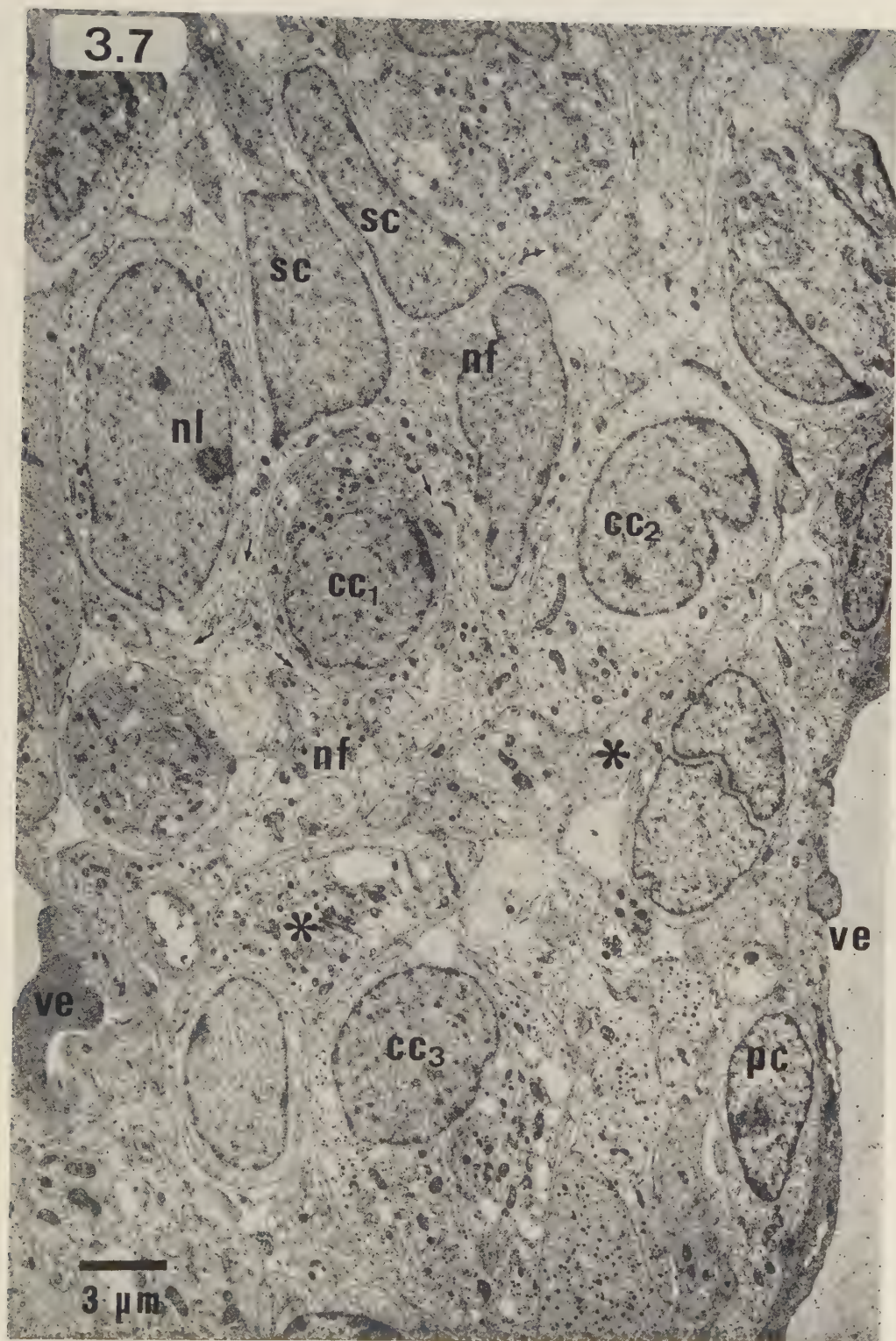


Fig. 3.8.

Relationship between supporting and chief cells. Carotid glomus cr 59.

Chief cell extensions (cc) invested, together with nerve fibres (nf), by supporting cells (sc) and their extensions (arrows). The supporting cells contain scanty perinuclear cytoplasm with few organelles.

Magnification: $\times 9,400$.

Fig. 3.9.

Chief cell and its relations. Carotid glomus cr 59.

The nucleus of the chief cell is asymmetrical in the cytoplasm and contains a nucleolus (nl) and chromatin fragments (ch) particularly dense beneath the nuclear membrane. On the side with ample cytoplasm stacks of Golgi cisterns (g) and granular endoplasmic reticulum (ger). The cell is invested partly by a supporting cell (sc) adapting its shape to the circumference of the chief cell, partly by supporting-cell processes (arrow), and partly by a chief-cell process (asterisk). Configurations like this and the one shown in Fig. 3.8 afford the impression that the relationship of the chief cells to the supporting cells is easiest to analyse when the chief cell is conceived as an axon in relation to its Schwann cell.

Magnification: $\times 10,300$.

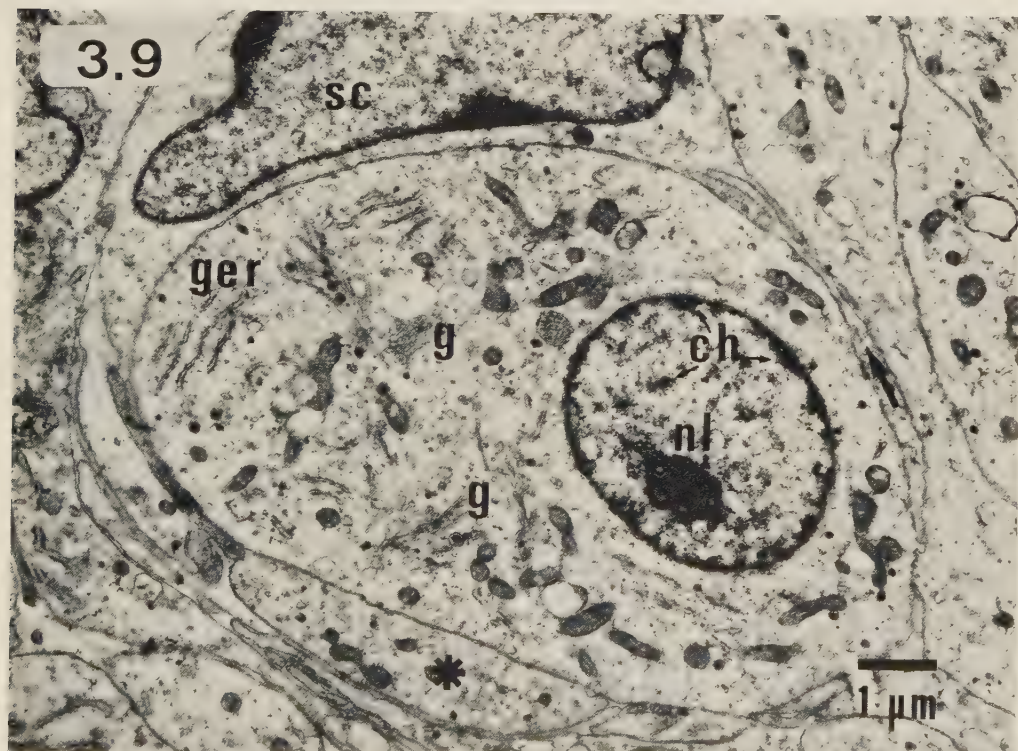
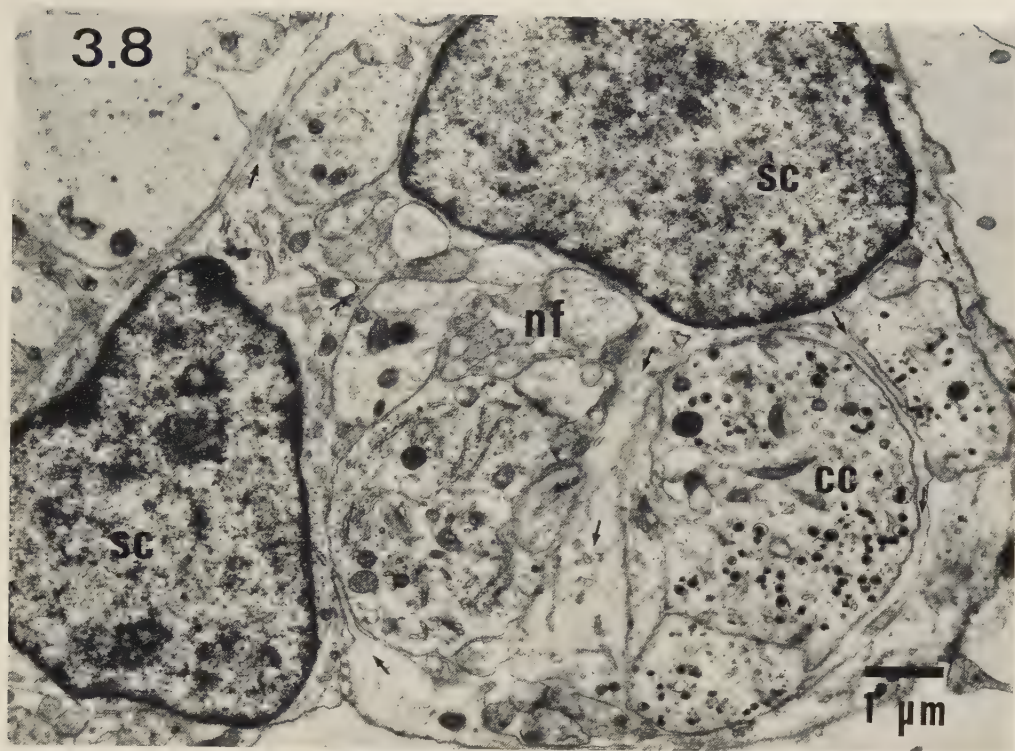


Fig. 3.10

Electron microscopic low power view of a region with vessels. Carotid glomus cr 59.

A group of chief and supporting cells (cc, sc) situated paravascularly. Between the vessel (ve) and the glomus cells a pericyte (pc).

Magnification: $\times 5,200$.

Fig. 3.11.

Endothelial pores. Carotid glomus cr 59.

Magnification of the area framed in Fig. 3.10, with vascular lumen (ve), endothelium (en), with fenestra (arrows) and a pericyte (pc).

Magnification: $\times 41,000$.

Fig. 3.12.

Endothelial pores. Carotid glomus cr 61.

While in Figs. 3.10 and 3.11 there is a considerable distance between vessel and chief cell, the chief cell (cc) in the area illustrated here is delimited from the vascular lumen only by fenestrated endothelium (en, arrows), a cell process (thick arrow), and an interstitial space (is). No material for a basal lamina has developed around the endothelium.

Magnification: $\times 74,100$.

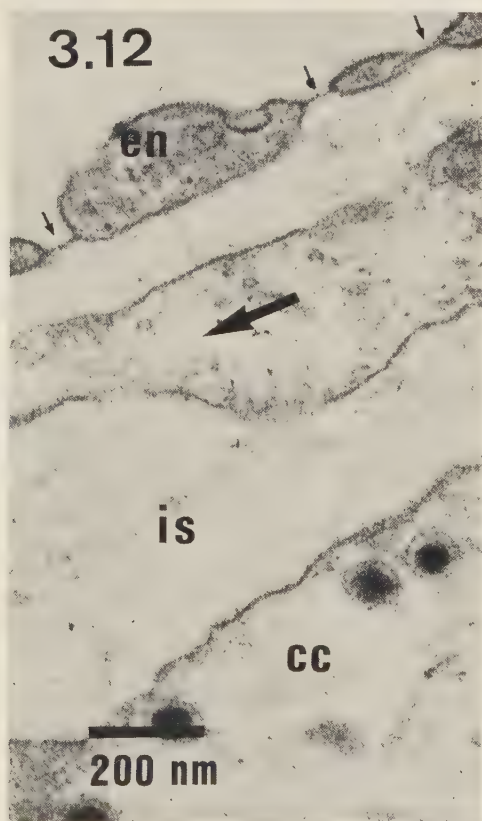
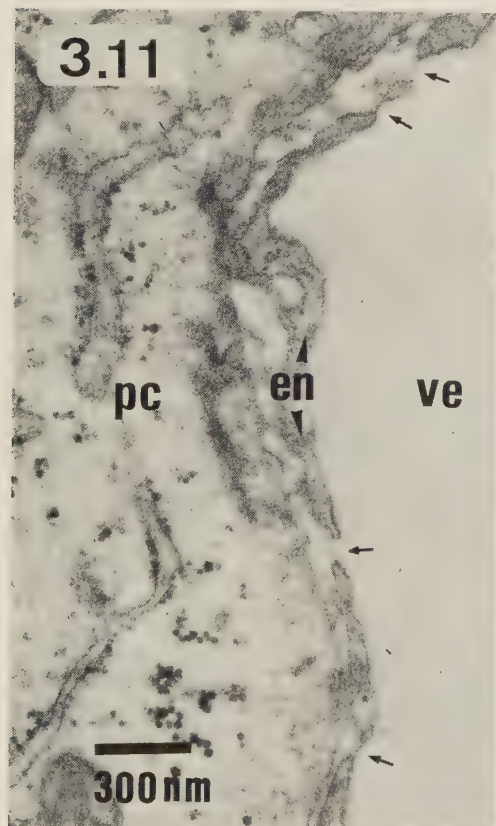
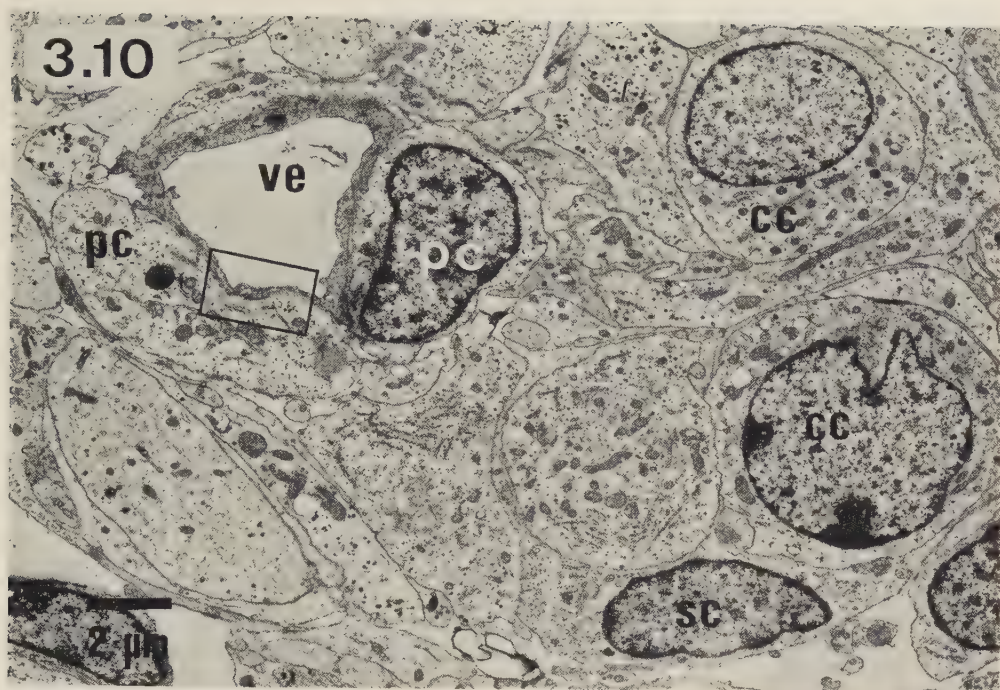


Fig. 3.13.

Organelles in a chief cell. Carotid glomus cr 55.

Granular endoplasmic reticulum (ger) densely studded with ribosomes which also occur free and if so mainly in the form of polyribosomes (r). Golgi complex (g), mitochondria (m), electron opaque body (db), specific granules (sg), microtubule (mt). The membrane-bound, pale vacuoles (1-5) may have formed from the outer, greatly folded nuclear membrane (1), from the Golgi cisterns (2), by dilatation of cisterns belonging to the granular (3) or the agranular (4) endoplasmic reticulum, or by vacuolation of mitochondria (5).

Magnification: $\times 27,500$.

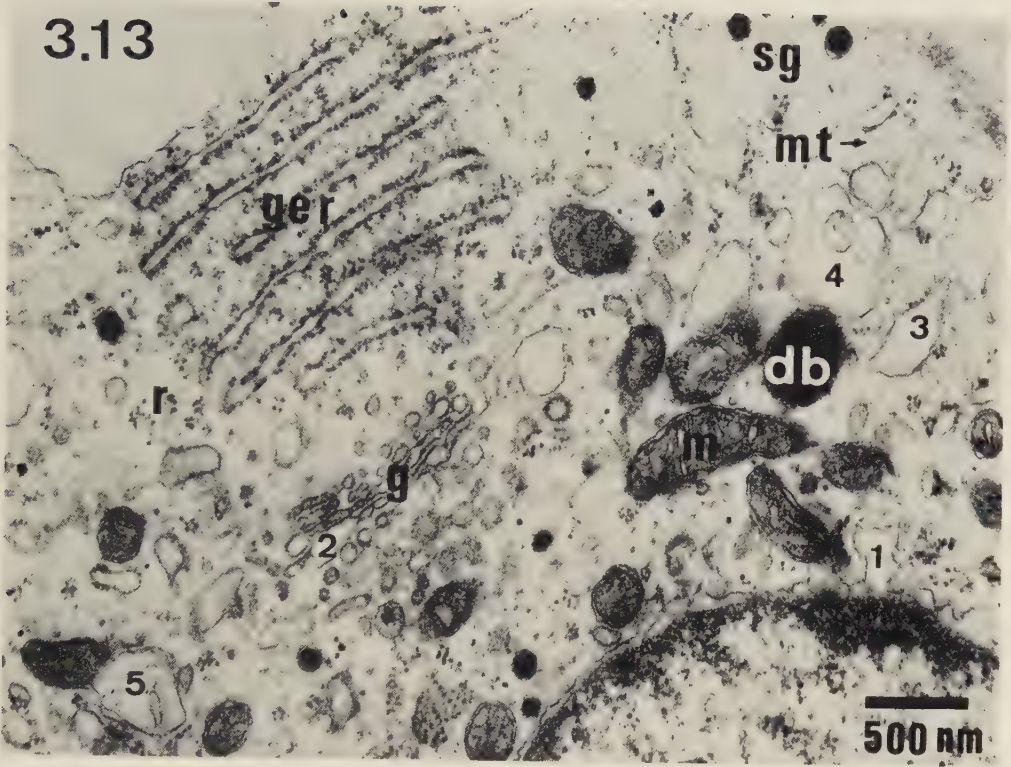
Fig. 3.14.

Detail of chief cell. Carotid glomus cr 55.

The specific granules (sg) exhibit varying size. This may be ascribed partly to the granules having been obliquely cut close to their centre (sg_1) or peripheral to the centre (sg_2 , sg_3). Structures like those marked sg_4 presumably represent granules which have been cut so peripherally that the electron-opaque core has not been hit; therefore, only the vesicles are visible. At the origin of a chief cell process (pcc) microtubules convene (mt). Where the chief cell adjoins other cells (thick arrows) there is an intercellular space, about 30 nm, of uniform width. In a small area at the base of the chief cell process the plasmalemma adjoins a major intercellular interstice (is).

Magnification: $\times 90,000$.

3.13



3.14

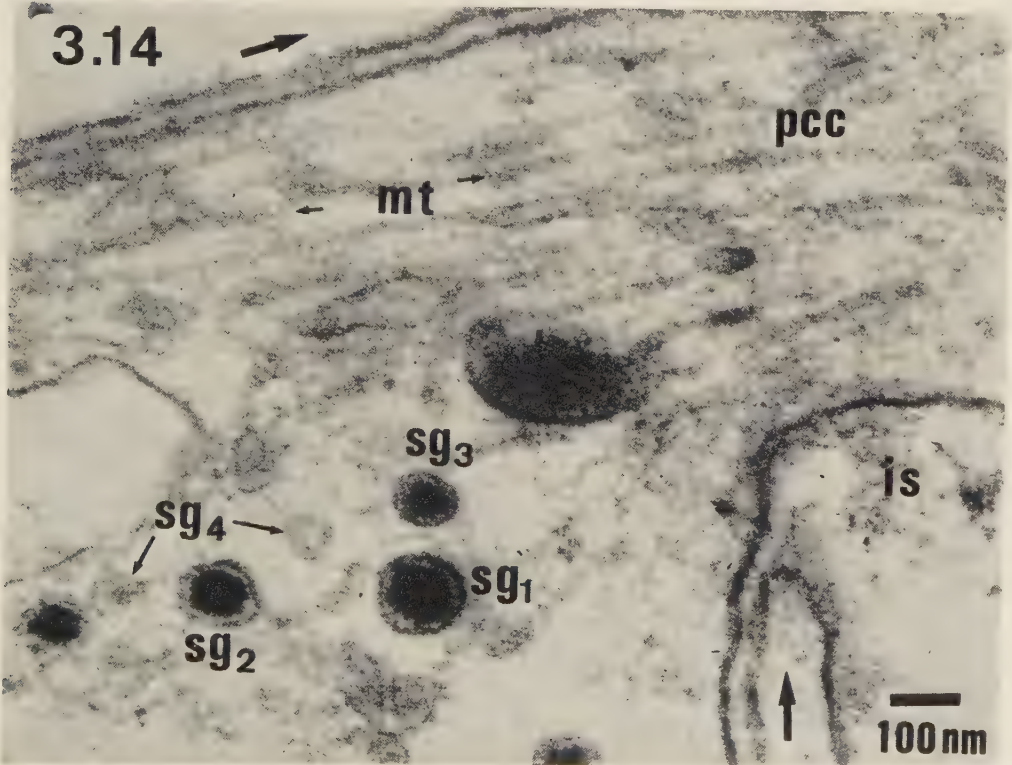


Fig. 3.15.

Detail of chief cell. Carotid glomus cr 55.

Desmosome-like plasma membrane changes (d). Partially ribosome-studded cistern from the endoplasmic reticulum (r), laminated, membrane-bound body (lb). The nuclear pore (np) closes the perinuclear cistern. Central to the pore there is a break in the chromatin fragments (ch) beneath the inner nuclear membrane.

Magnification: $\times 63,000$.

Fig. 3.16.

Detail of chief cell. Carotid glomus cr 55.

Multivesicular body (vcb), vacuole (va), mitochondrion with mitochondrial granule (mg). Solitary ribosomes (r_1), polyribosomes (r_2), membrane-bound ribosomes (r_3).

Magnification: $\times 54,000$.

Fig. 3.17.

Detail of glomus cell. Carotid glomus cr 62.

Cilia-like process (ci) in a not definitely identified cell.

Magnification: $\times 54,200$.

Fig. 3.18.

Detail of chief cell. Carotid glomus cr 62.

Desmosome (d-d), micropinocytotic process (mpv), specific granules (sg).

Magnification: $\times 79,800$.

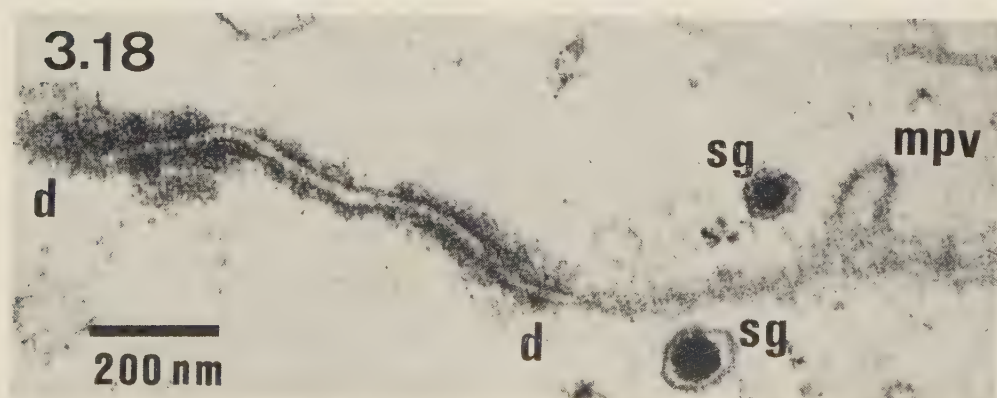
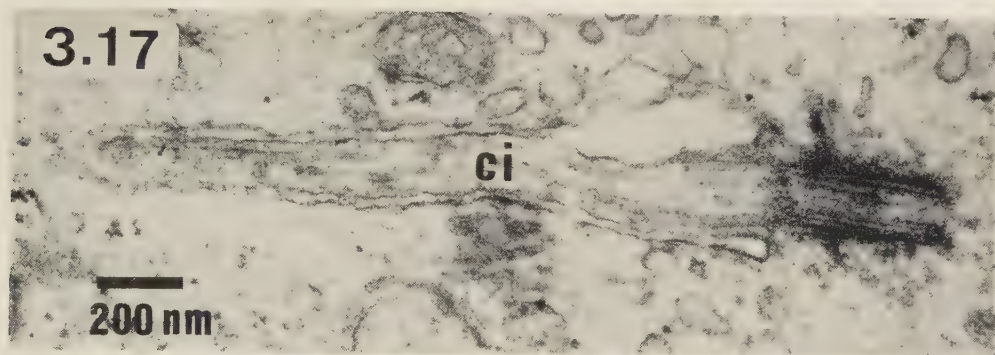
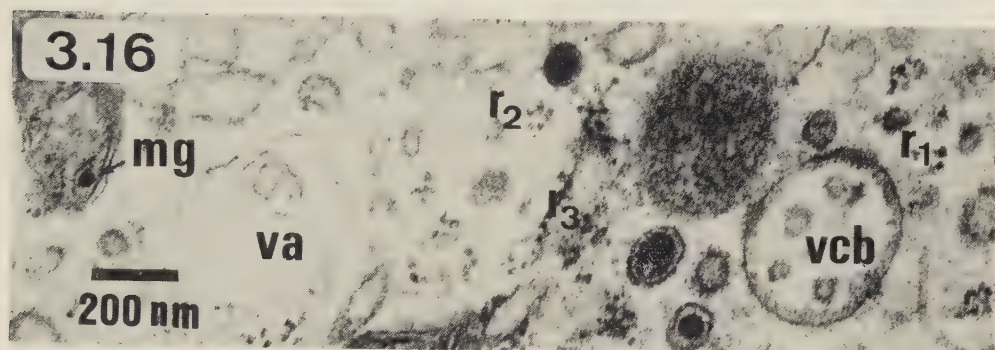
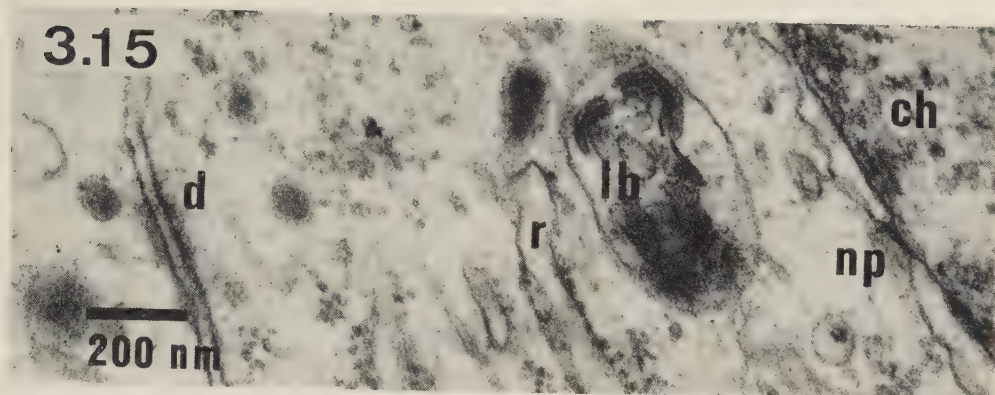


Fig. 3.19.

Nerve fibres between glomus cells. Carotid glomus cr 62.

Nerve fibres (nf) of varying thickness with longitudinal neurotubules interposed between chief cells (cc) separated by supporting cell processes (arrows). No accumulation of synaptic vesicles or mitochondria in the nerve fibres or in the cells close to the nerve fibres, and no thickening of the plasma membranes where cells and nerve fibres adjoin.

Magnification: $\times 54,200$.

Fig. 3.20.

Nerve fibres between glomus cells. Carotid glomus cr 62.

Between two chief cells (cc) joined by desmosome (d) is inter-digitated a supporting cell process (arrows) and a nerve fibre (nf) containing neurotubules and a small mitochondrion.

Magnification: $\times 44,600$.

Fig. 3.21.

Detail of Golgi complex in a chief cell. Carotid glomus cr 59.

The illustrated Golgi zone is predominated by partially communicating cisterns. One, at the terminal end (long arrow) contains material of an appearance like that in the specific granules (sg). Golgi vesicle (vs).

Magnification: $\times 108,000$.

Fig. 3.22.

Specific granules in a chief cell. Carotid glomus cr 62.

A typical specific granule (sg_1) containing an almost circular, homogeneous, very electron-opaque core (1) surrounded by a membrane which is trilaminar (3). Between the core and the vesicle a space (2) containing a material which is less electron transparent than the cytoplasmic ground substance and which in many places contains small granules reminiscent of core material. The nuclei vary in shape and size (sg_2 , sg_3), but their basic architecture is always that described above.

Magnification: $\times 188,000$.

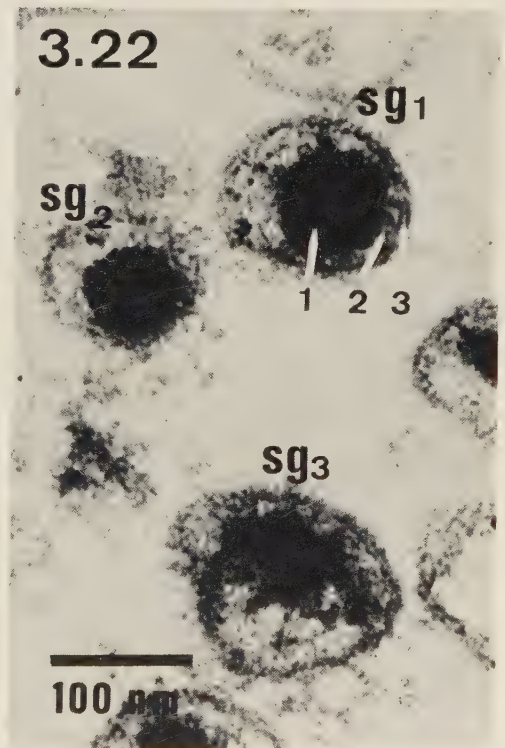
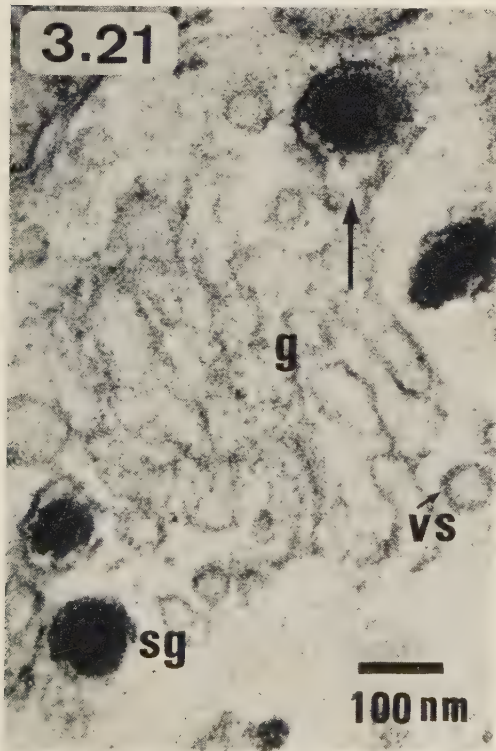
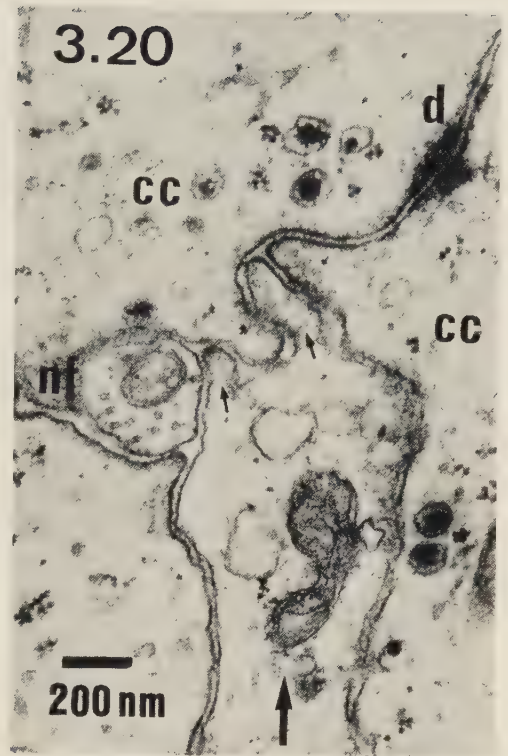
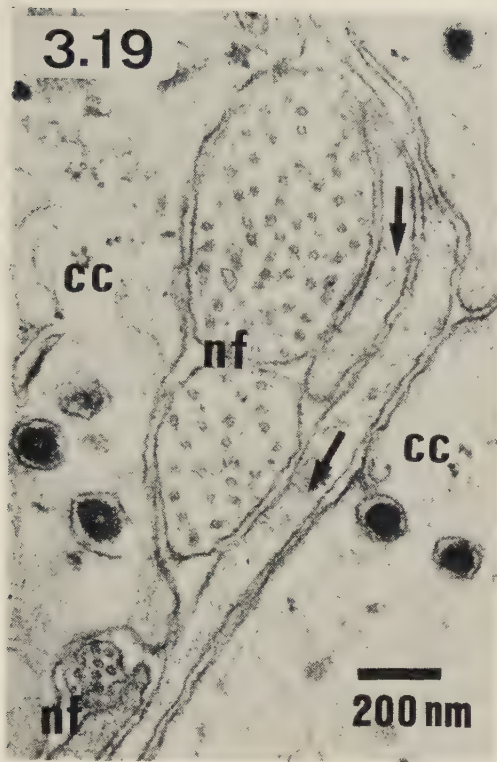


Fig. 4.1.

Light microscopic low power view. Inferior aorticopulmonary glomus cr 55.

Section through the bifurcation of the pulmonary trunk showing the inferior aorticopulmonary glomus (2) in the mesenchyme between the ascending aorta (1) and the pulmonary trunk (4). The vessel (3) to the glomus penetrates the wall of the pulmonary trunk.

Magnification: $\times 64$.

1. Ascending aorta.
2. Inferior aorticopulmonary glomus.
3. Glomus vessel.
4. Pulmonary trunk.
5. Right pulmonary artery.
6. Left pulmonary artery.

Fig. 4.2.

Light microscopic micrograph. Inferior aorticopulmonary glomus cr 55.

Magnification of a low power view from the glomus shown in Fig. 4.1 following ultrasectioning for five grids. The glomus is predominated by cells having oval nuclei (3) and a delicately granular cytoplasm. A few cells have irregular and angular nuclei and apparently but little perinuclear cytoplasm (2). The glomus cells adjoin a nerve (1), vessel (4), ganglion cells (5), and fibroblasts (6).

Magnification: $\times 640$.

1. Bundle of nerve fibres.
2. Supporting cell.
3. Chief cell.
4. Vessel.
5. Ganglion cells.
6. Fibroblasts.

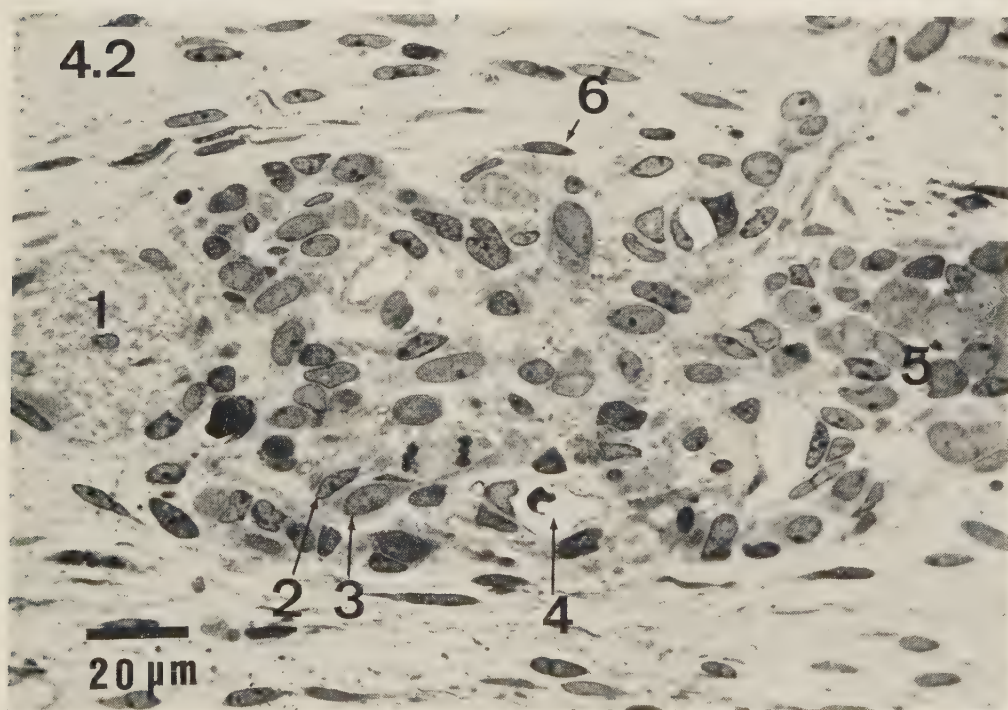
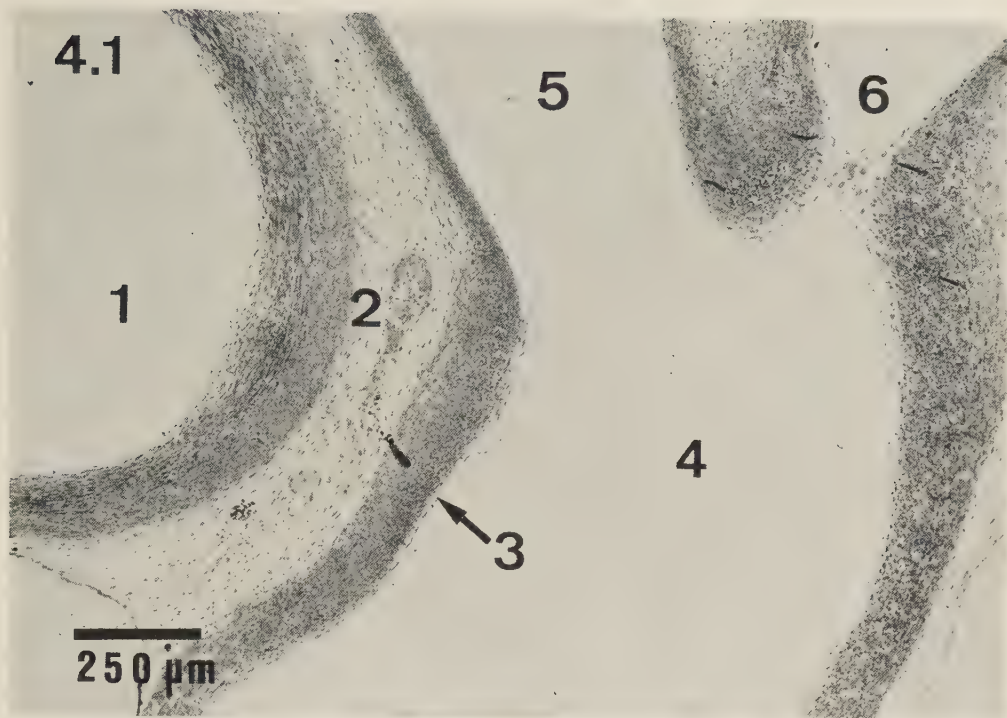


Fig. 4.3.

Electron microscopic low power view. Inferior aorticopulmonary glomus cr 61a.

Between two vascular lumina (ve) granular chief cell (cc) and supporting cells (sc). The granule content of the chief cells is varying. Nucleolus in the chief cell (nl).

Magnification: $\times 3,600$.

Fig. 4.4.

Electron microscopic low power view. Inferior aorticopulmonary glomus cr 55.

A supporting cell (sc) giving off long processes (arrows) embracing two chief cells (cc). Nerve fibres (nf) and pale (cc₁) as well as dark (cc₂) chief-cell extensions coursing between the cells. Around the cell group fibroblast processes (fb) and collagen fibres (cf).

Magnification: $\times 3,800$.

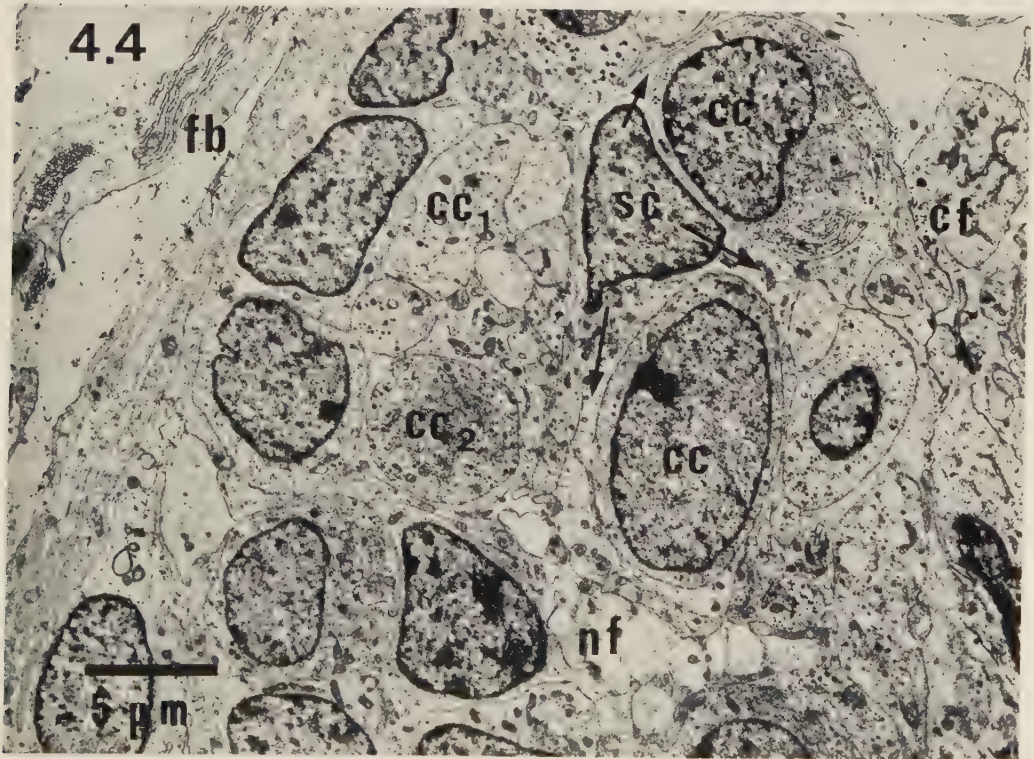
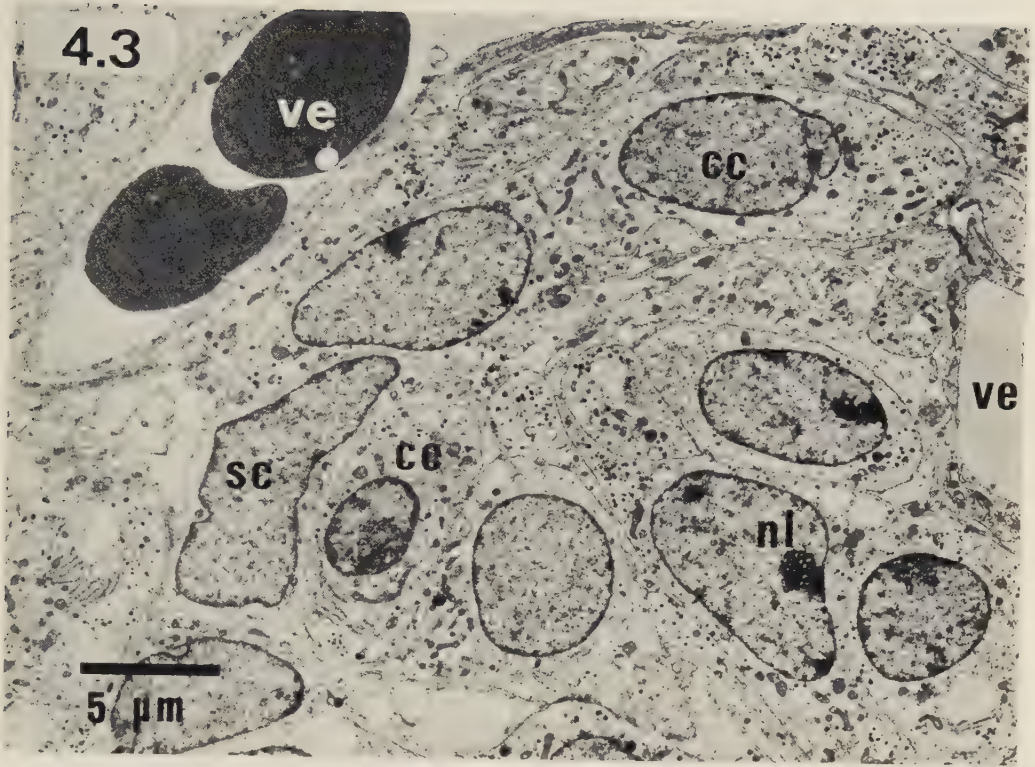


Fig. 4.5.

Moderately high power electron microscopic view of a supporting cell. Inferior aorticopulmonary glomus cr 55.

The supporting cell (sc) with its processes (arrows) invests two-thirds of the chief cell (cc). The remaining third of the chief cell plasmalemma adjoins other chief cells or nerve fibres (nf₁, nf₂). In the cytoplasm of the supporting cell mitochondria (m), Golgi complex (g), free and membrane-bound ribosomes (r), and a pale vacuole (va) whose interior communicates with the perinuclear cistern of the cell. The nucleus of the supporting cell is indented by the chief cell and by neighbouring nerve fibres (nf₃).

Magnification: $\times 14,000$.

Fig. 4.6.

Magnification of the area around nf₁ in Fig. 4.5. Inferior aorticopulmonary glomus cr 55.

At the site of contact between the supporting-cell process extension (thick arrow), the chief cell, and the nerve fibre there are no signs of synaptic specialization. Transversely cut neutrotubules in the nerve fibre (nt) and transversely cut microtubules in the chief cell (mt) show the same diameter. Nuclear pores (np), perinuclear chromatin (ch).

Magnification: $\times 65,000$.

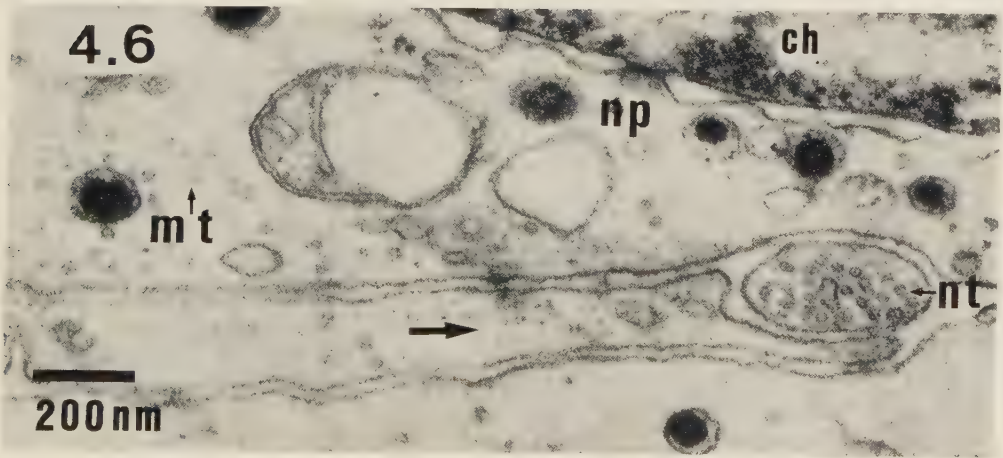
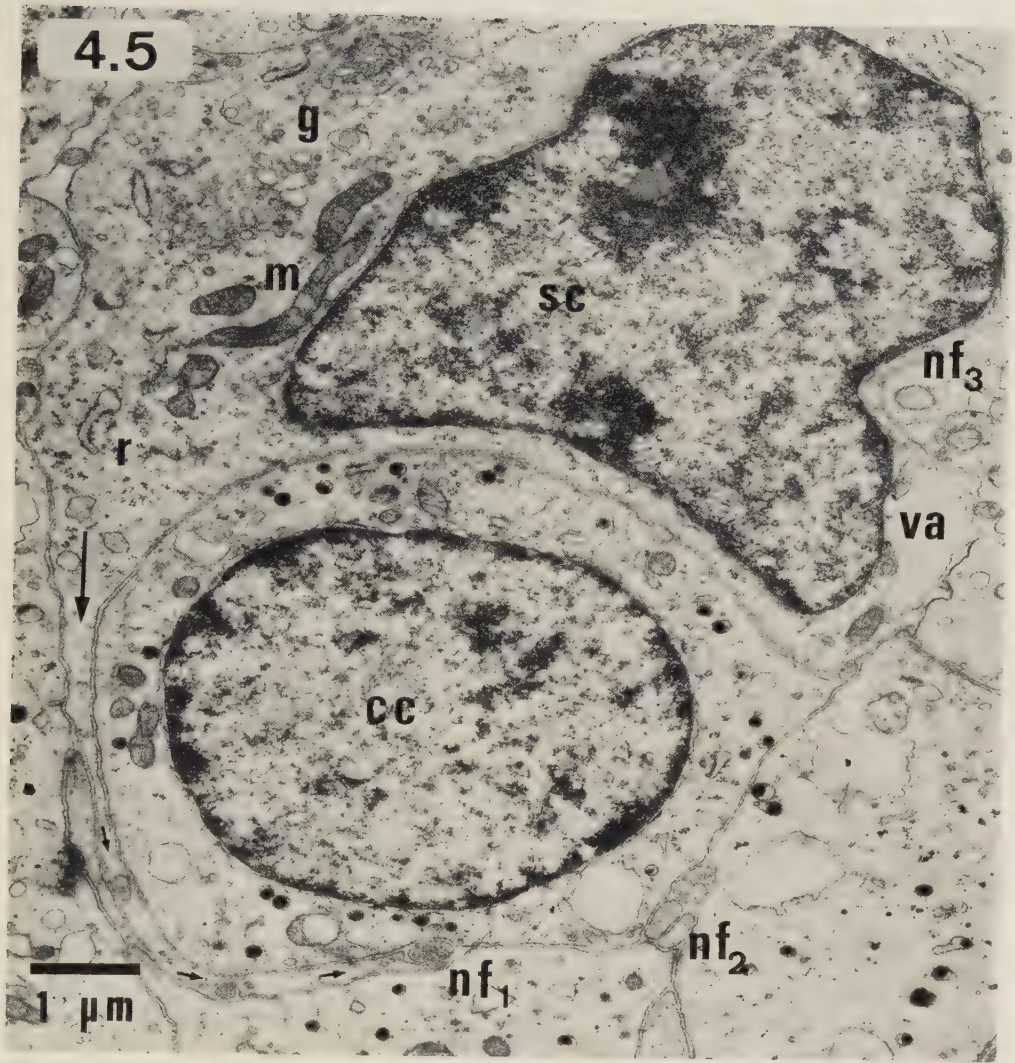


Fig. 4.7.

Moderately high power electron microscopic view of a chief cell. Inferior aorticopulmonary glomus cr 62.

The nucleus (nu) is of a slightly irregular shape. In the cytoplasm a Golgi zone (g), mitochondria (m), vacuoles (va), ribosomes (r), and osmiophilic granules (sg). In the part of the chief cell (cc) which is at the bottom on the right the cytoplasm is somewhat paler.

Magnification: $\times 12,800$.

Fig. 4.8.

Moderately high power electron microscopic view of part of a chief cell. Inferior aorticopulmonary glomus cr 59.

Accumulation of osmiophilic granules (sg), granular endoplasmic reticulum (ger), mitochondria (m), desmosome (d). The mitochondria as well as the vesicles of the granules are vacuolated, presumably due to insufficient fixation.

Magnification: $\times 12,200$.

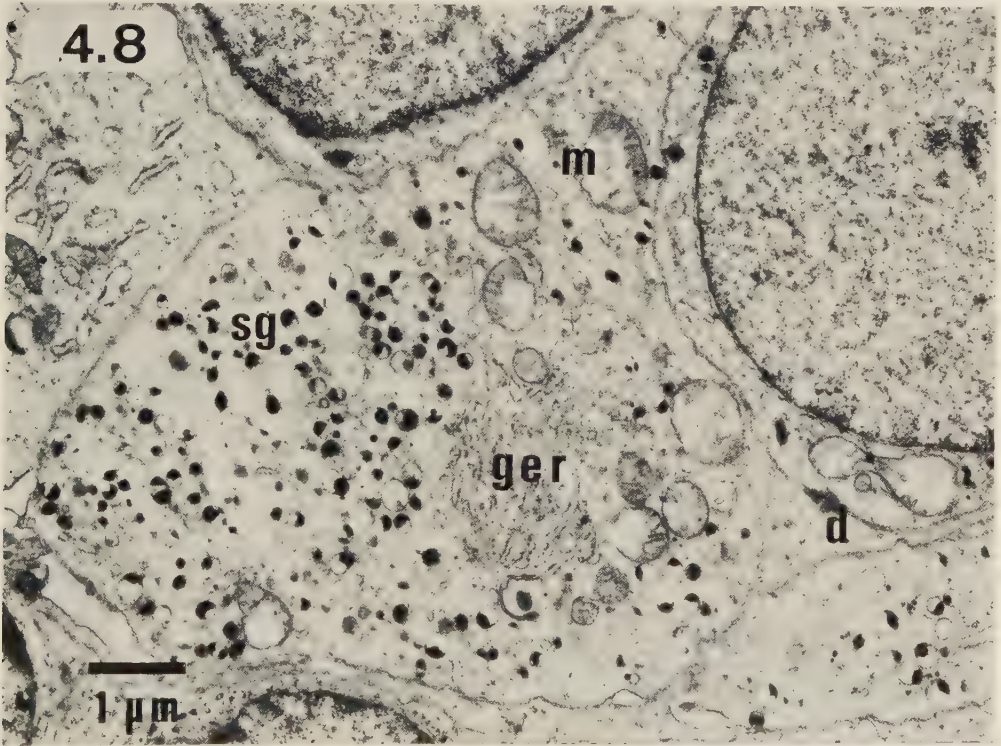
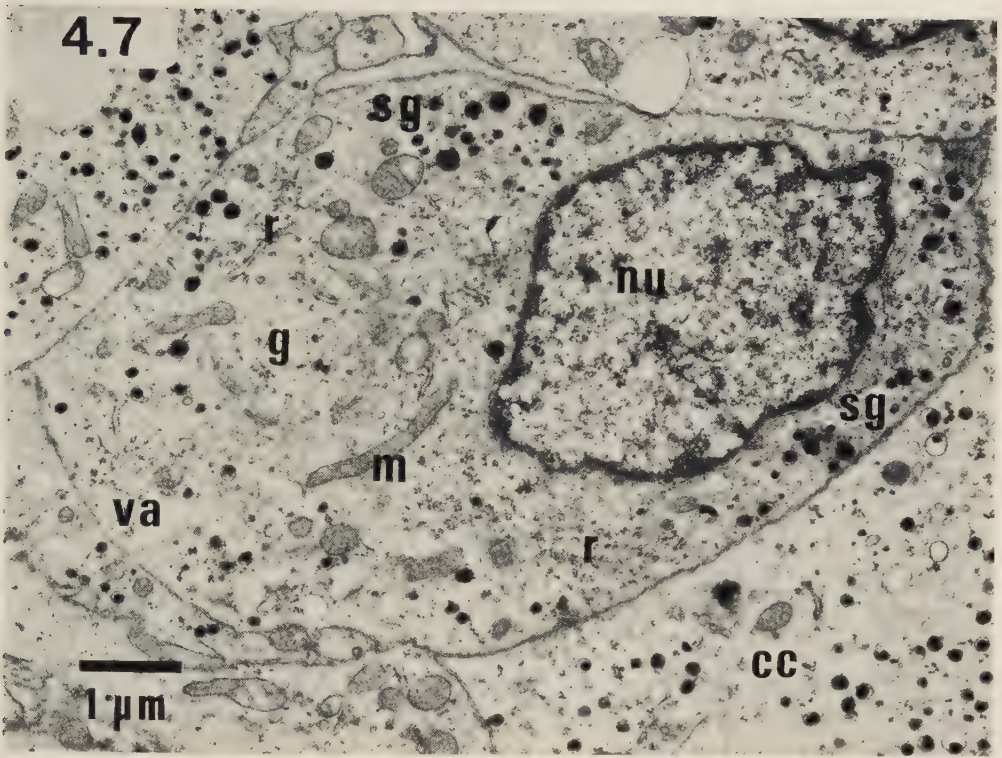


Fig. 4.9.

Vessel with pericyte. Inferior aorticopulmonary glomus cr 61a.

Between the vascular lumen (lu) and the chief cell (cc) there are parts of a supporting cell (at 1) or parts of a supporting cell and a pericyte (at 2). Endothelial cell nucleus (en), pericyte (pc), and a free chief-cell process (pcc).

Magnification: $\times 8,500$.

Fig. 4.10.

Endothelial pores. Inferior aorticopulmonary glomus cr 61a.

Endothelium with pores (ep) delimited from the chief cell (cc) by a cell process (sc).

Magnification: $\times 50,600$.

Fig. 4.11.

Endothelial pore. Inferior aorticopulmonary glomus cr 62.

No interposed cell parts between the fenestrated endothelium (ep) and the chief cell (cc).

Magnification: $\times 57,000$.

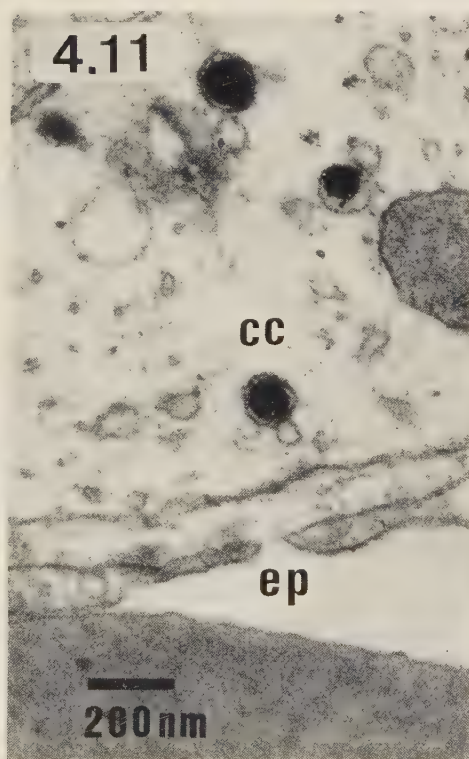
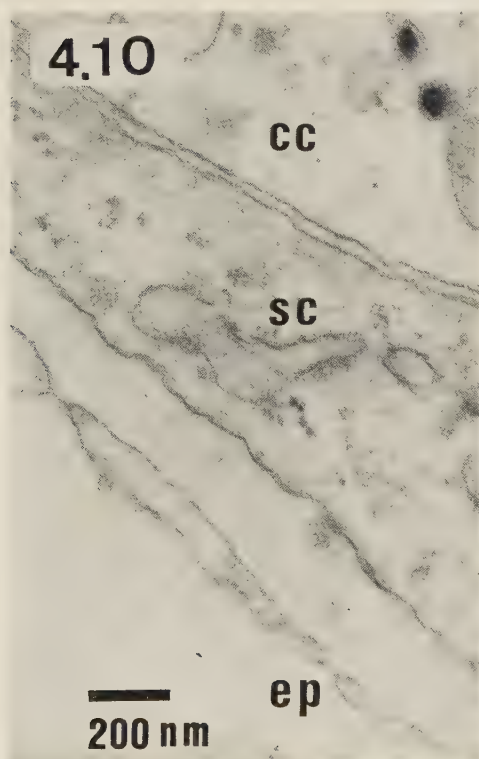
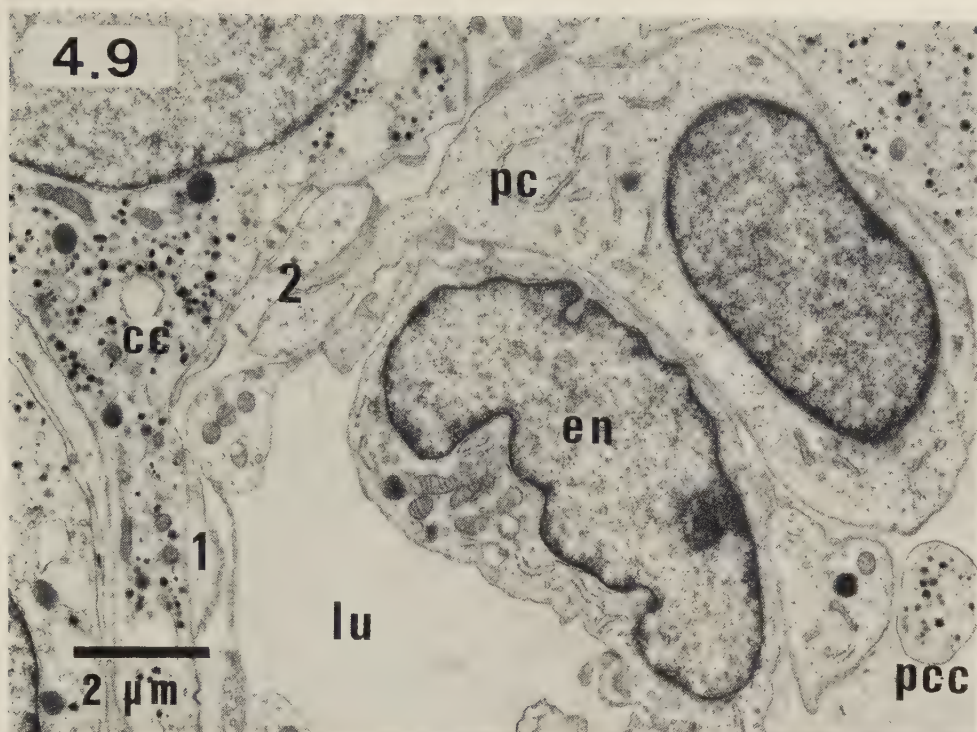


Fig. 4.12.

Detail of chief cell. Inferior aorticopulmonary glomus cr 61a.

Golgi complex (g), cilium (ci), specific granules (sg).

Magnification: $\times 37,100$.

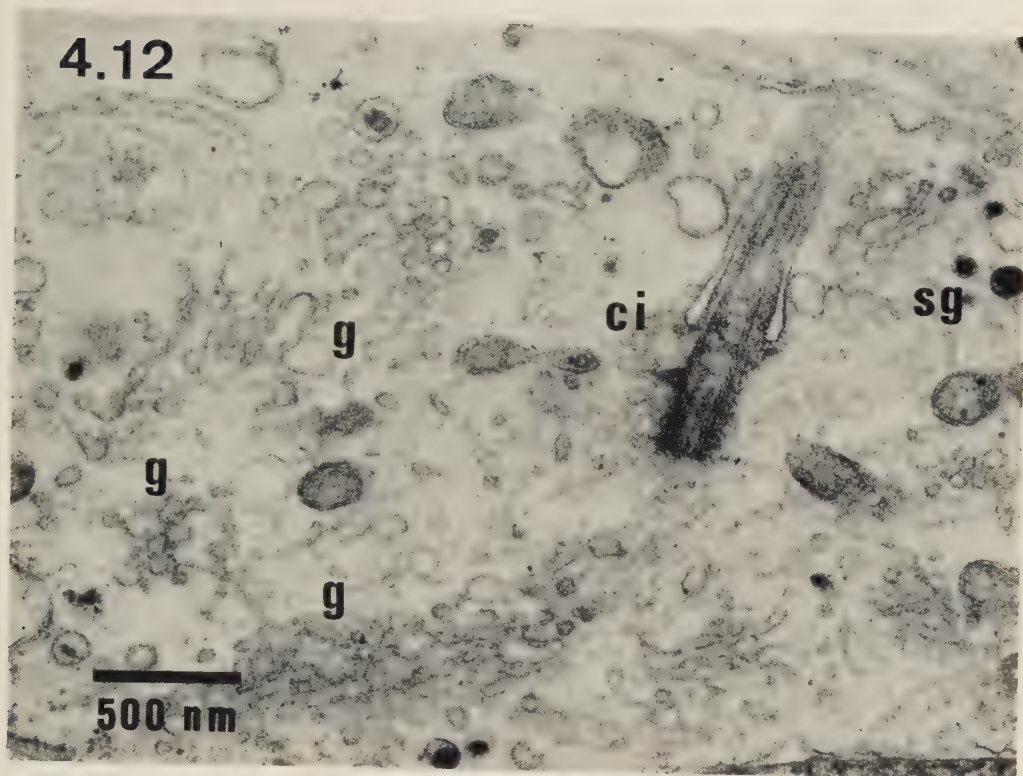
Fig. 4.13.

Detail of chief cell. Inferior aorticopulmonary glomus cr 61b.

In the zone between cisterns belonging to the granular endoplasmic reticulum (ger) and cisterns belonging to the Golgi complex (g) small vesicles (between the arrows). Dilated mitochondrion (m), mitochondrion with granule (mg), specific granules (sg), unidentified vacuole (va), polyribosomes (r).

Magnification: $\times 47,300$.

4.12



4.13

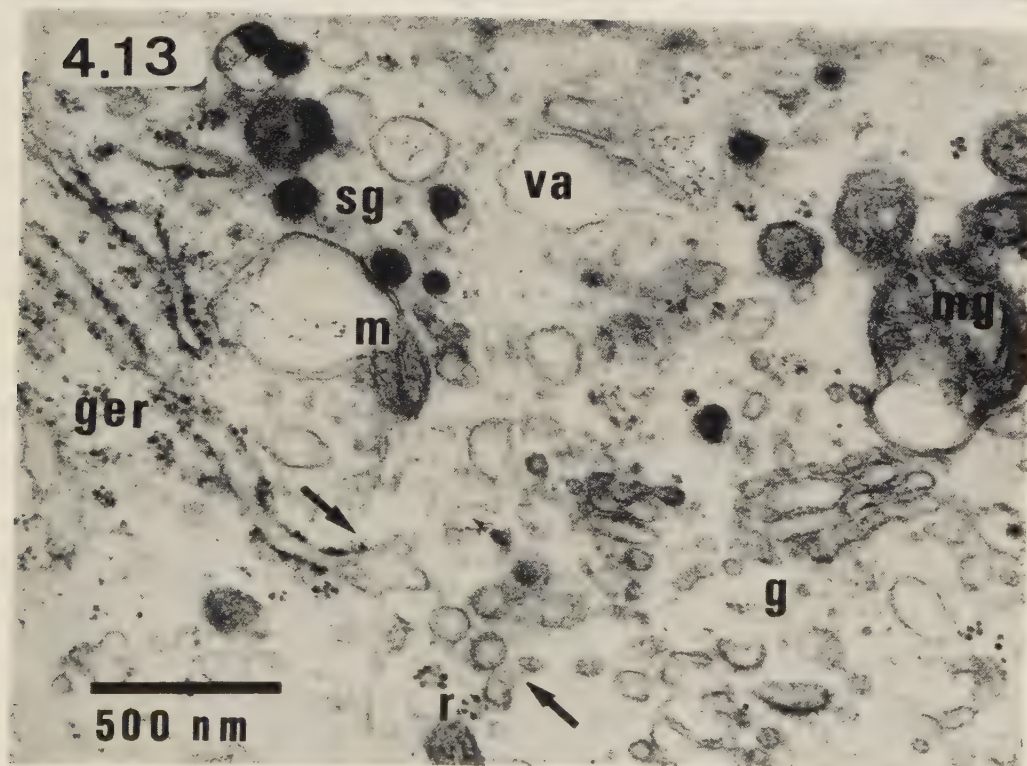


Fig. 4.14.

Detail of Golgi zone in a chief cell. Inferior aorticopulmonary glomus cr 55.

In the Golgi cisterns (g) in several places accumulations of a material (arrows) of approximately the same density as the core in the specific granules (sg). Multi-vesicular body (vcb).

Magnification: $\times 76,500$.

Fig. 4.15.

Detail from the Golgi zone in a chief cell. Inferior aorticopulmonary glomus cr 59.

The end of one of the Golgi cisterns (g) distended and containing a material of an appearance like that of the cores of the specific granules (arrows).

Magnification: $\times 114,000$.

Fig. 4.16.

Nerve fibres. Inferior aorticopulmonary glomus cr 61a.

The nerve fibres (nf) are embedded between a chief cell (cc) and a supporting cell (sc). Electron-opaque body (db).

Magnification: $\times 41,600$.

Fig. 4.17.

Detail of a chief-cell process. Inferior aorticopulmonary glomus cr 55.

In one granule (sg_4) the vesicular membrane is tightly wrapped about its core. In most other granules the vesicles seem to be dilated (sg_1), and the electron-opaque nucleus is of an asymmetric situation in the vesicle. The contents in the space between the core and membrane are pale, but interspersed with small electron-dense granules (sg_3) or thin filaments (sg_2). Longitudinally cut, parallel microtubules (mt).

Magnification: $\times 78,800$.

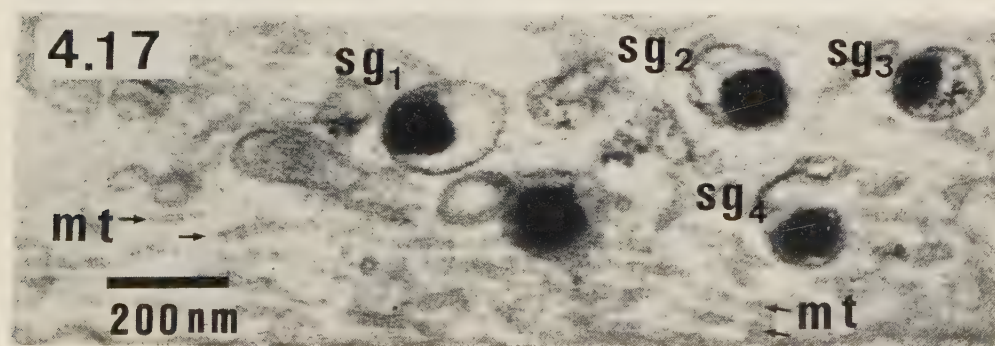
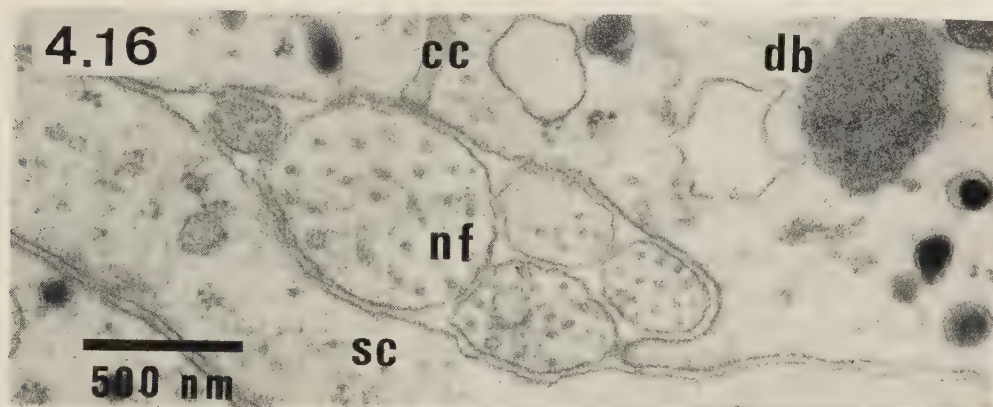
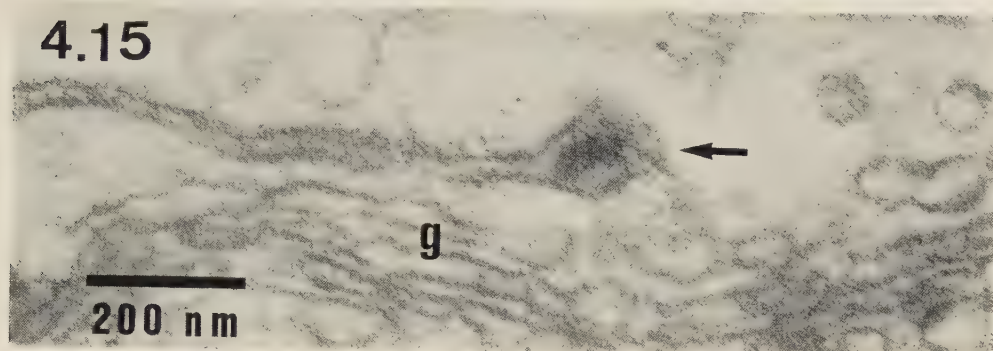
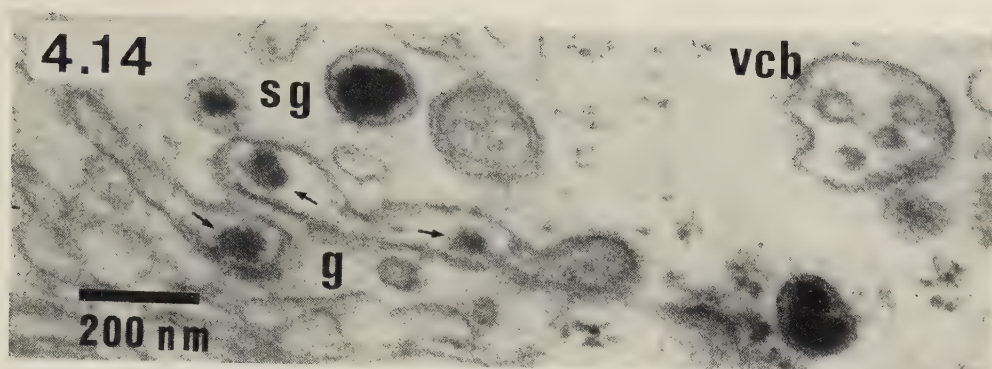


Fig. 4.18.

Light microscopic low power view. Middle aorticopulmonary glomus cr 59.

The glomus (3,4) is lying in loose mesenchyme between the ascending aorta (2), the left main bronchus (1), and the ductus arteriosus (5) cranial to the right pulmonary artery and caudal to the anterior part of the aortic arch. The right glomic lobe (3) represents the cranial part of a thin cellular process arising on a level with the right pulmonary artery. This extension is in this section adjoining a larger glomic lobe (4) considered to be the true middle aorticopulmonary glomus (cf. Fig. 4.30).

Magnification: $\times 64$.

1. Left main bronchus.
2. Ascending aorta.
- 3,4. Middle aorticopulmonary glomus.
5. Ductus arteriosus.
6. Left vagus nerve.

Fig. 4.19.

Light microscopic photomicrograph. Middle aorticopulmonary glomus cr 59.

Magnification of the framed area at 4 in Fig. 4.18. Between the cell clusters the vascular lumina (1) and mesenchyme (2). Among the cells a few (4) are lying in juxtaposition to other cells (3) or to vascular lumina (5).

Magnification: $\times 640$.

1. Vascular lumina with endothelial cells.
2. Interstitial mesenchyme.
3. Chief cells.
4. Supporting cells.
5. Pericyte.
6. Mitotic figure.

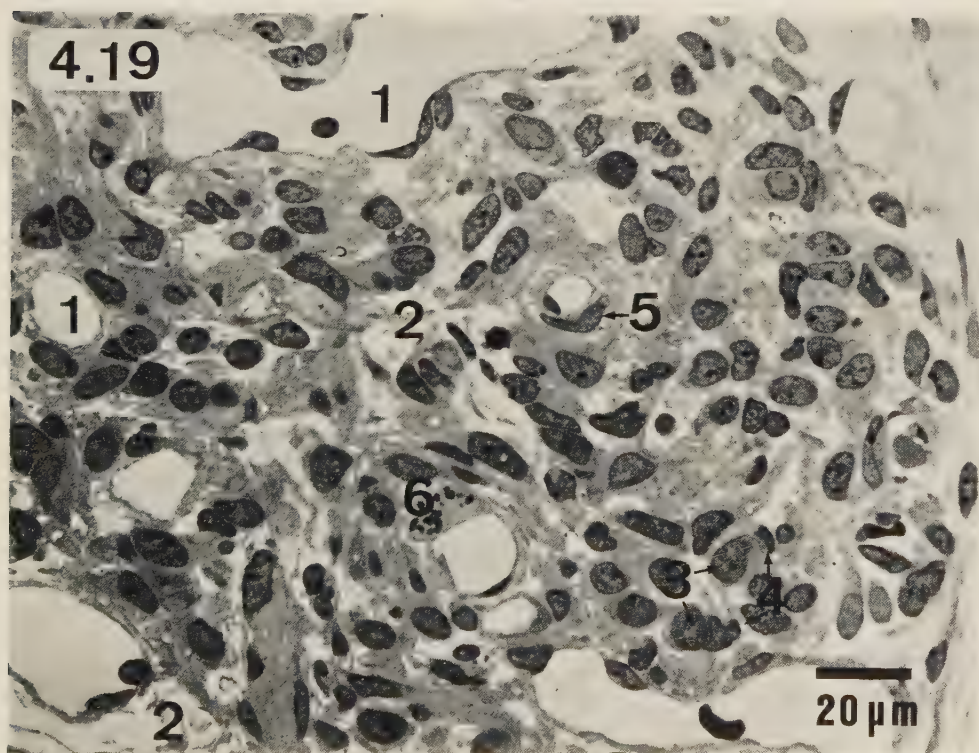
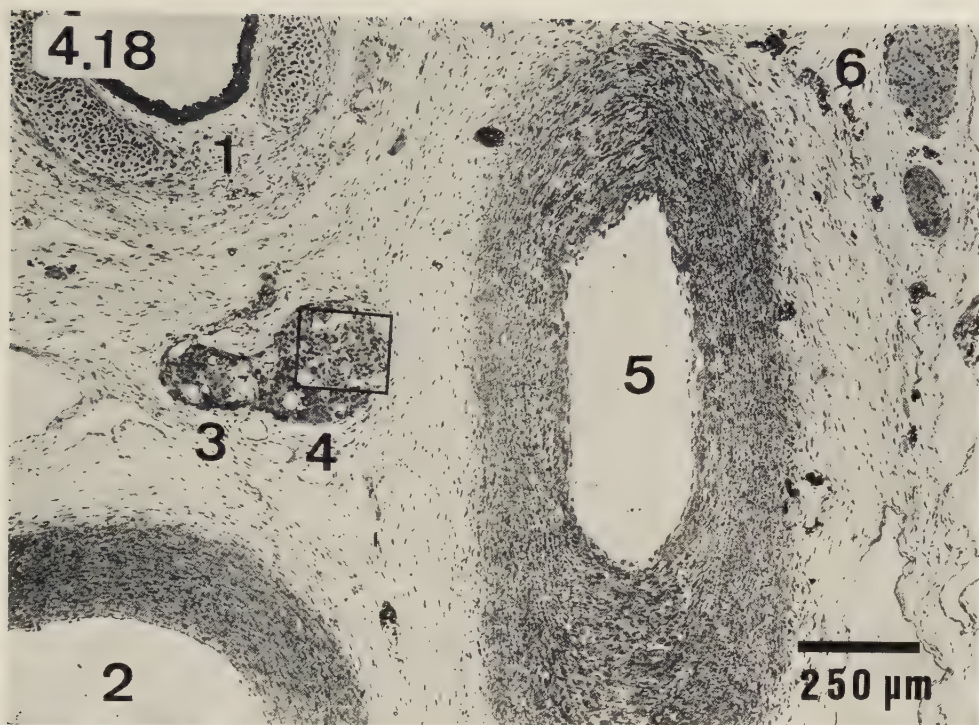


Fig. 4.20.

Electron microscopic low power view. Middle aorticopulmonary glomus cr 61a.

Granular chief cells (cc) predominate the picture, but there are a few supporting cells (sc) with cytoplasmic processes (arrows). In relation to the vessel (ve) a pericyte (pc) cut through the nucleus. Lastly, numerous cell fragments difficult to identify.

Magnification: $\times 3,800$.

4.20

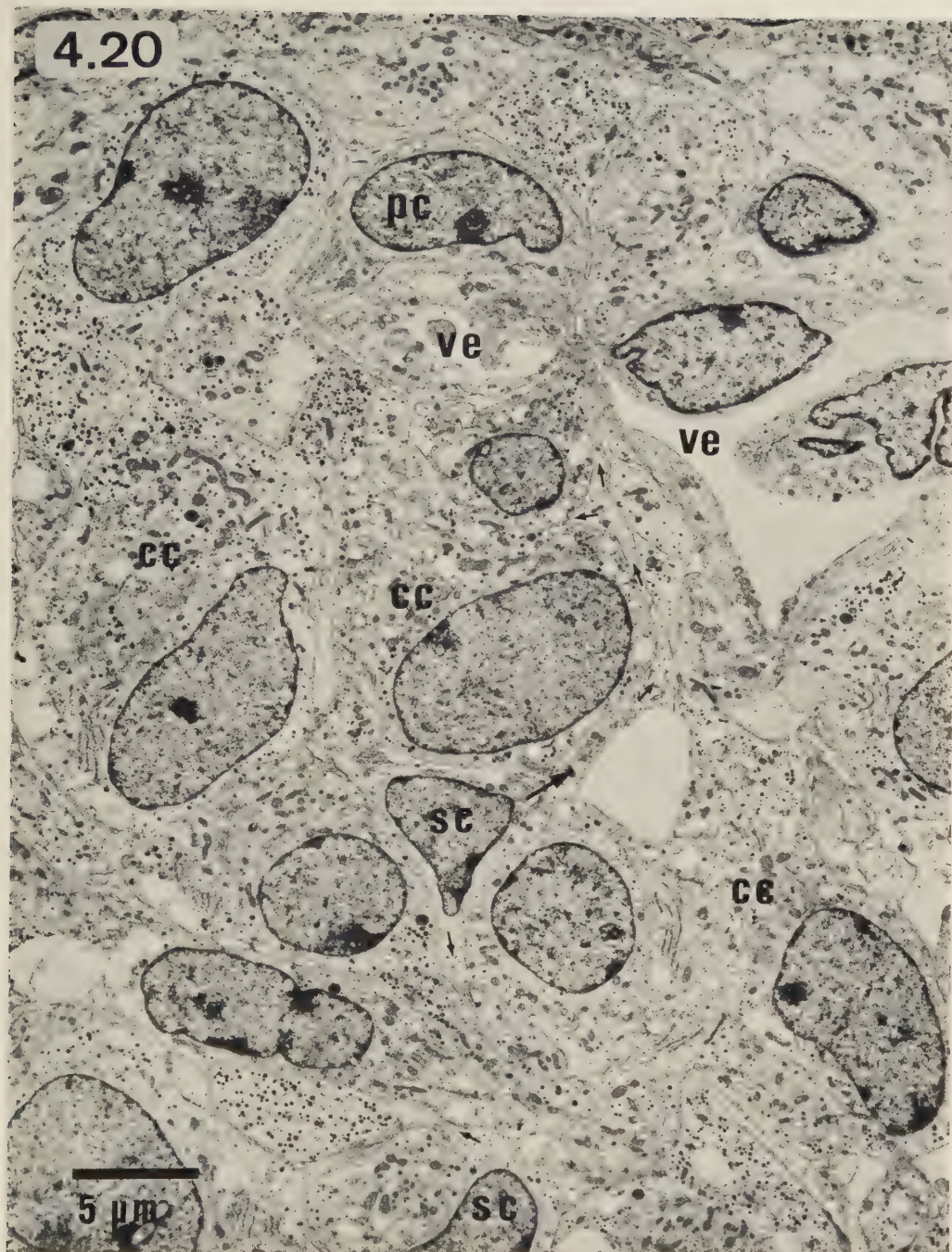


Fig. 4.21.

Relations of chief cell. Middle aorticopulmonary glomus cr 59.

Out of the three nuclei one belongs to a chief cell (cc) with a cytoplasmic extension (pcc) and the other two belong to supporting cells (sc). The chief cell is surrounded by numerous cytoplasmic processes several of which may be identified as nerve fibres (nf), others as chief-cell processes (asterisk) or supporting cells (arrow).

Magnification: $\times 7,900$.

Fig. 4.22.

Organelles in a chief cell. Middle aorticopulmonary glomus cr 59.

Nucleus (nu), granular endoplasmic reticulum (ger), mitochondria (m), vacuoles (va), some of which are vacuolated mitochondria (m_1), electron-dense body (db), Golgi complex (g), microtubules (mt). It will be noted that there is no accumulation of osmiophilic granules (sg) in the vicinity of the nerve fibres (nf).

Magnification: $\times 23,800$.

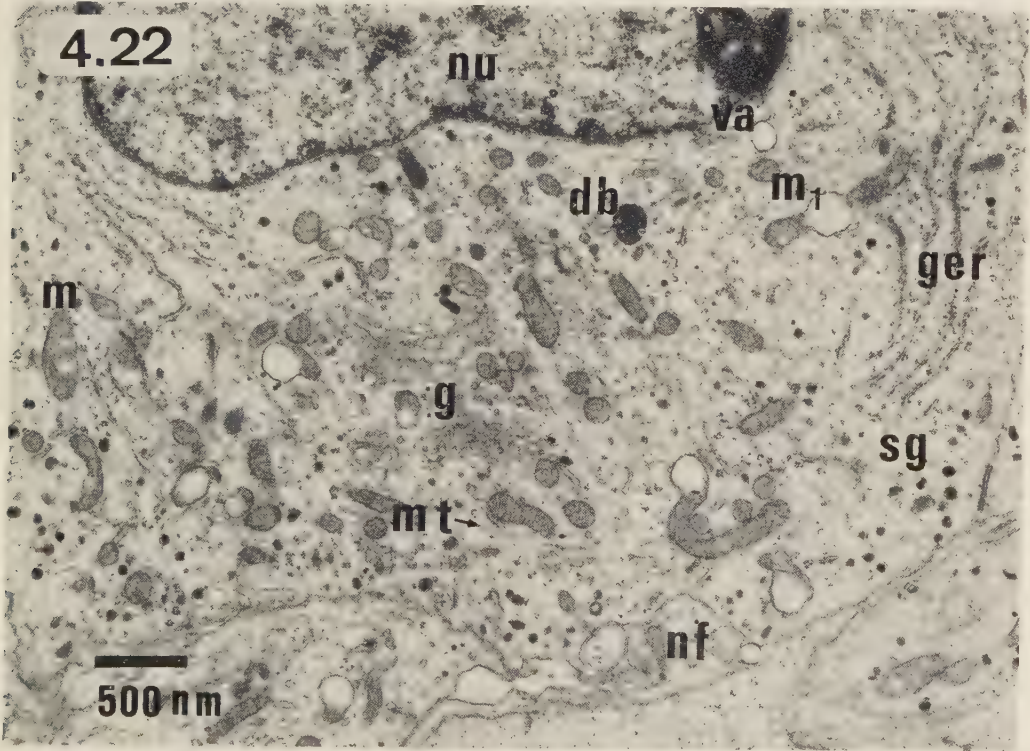
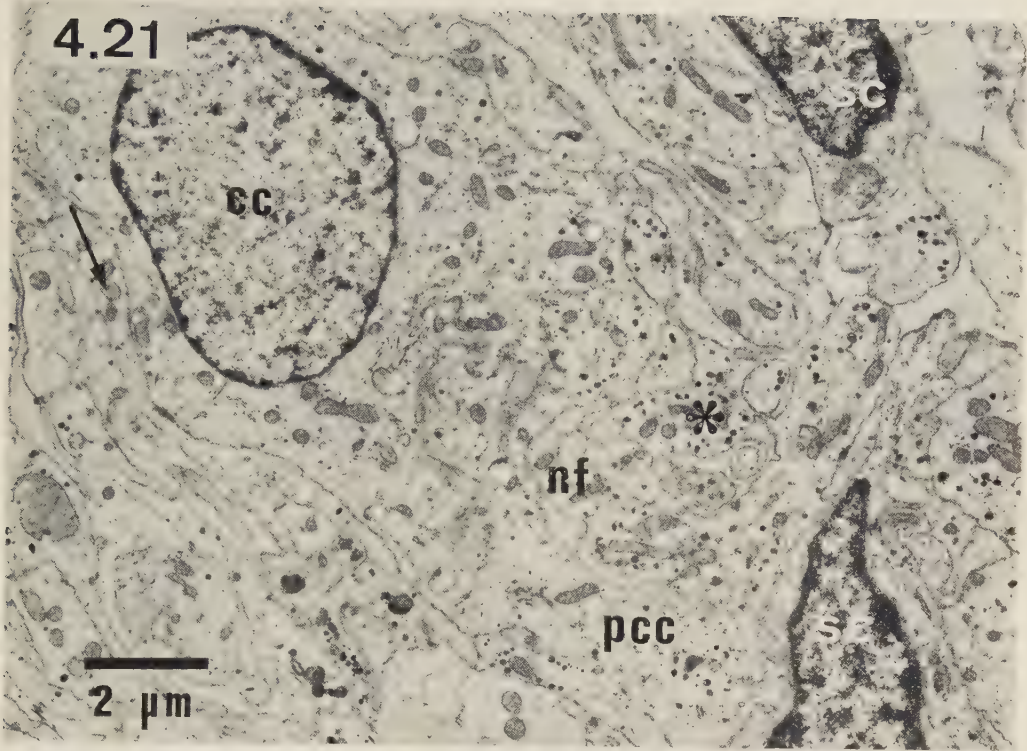


Fig. 4.23.

Supporting cell. Middle aorticopulmonary glomus cr 59.

In the perinuclear cytoplasm, around a supporting cell nucleus (sc), Golgi complex (g), electron-opaque body (db), and a few membrane-bound and free ribosomes (r). From the perinuclear cytoplasm long extensions (arrows) which almost completely invest the chief cell (cc). A secondary process partially envelops nerve fibres (nf₁). Other nerve fibres are embedded between chief-and supporting-cell processes (nf₂). An area of a chief cell uninvested by supporting cell (at is). Pericyte (pc). The framed area at the vascular lumen (ve) is magnified in Fig. 4.24.

Magnification: $\times 10,500$.

Fig. 4.24.

Endothelial fenestra. Middle aorticopulmonary glomus cr 59.

Endothelial pores (ep). Compared with Fig. 4.23 it will be seen that the chief cells are separated by these pores. Pericytes (pc).

Magnification: $\times 66,000$.

Fig. 4.25.

Endothelial fenestra. Middle aorticopulmonary glomus cr 61a.

Part of a chief cell cc₁ close to the endothelial fenestra (ep), but separated from them by paravascular cell processes (arrow 1). The chief-cell part cc₂ is further delimited from the vessel by a supporting-cell process (arrow 2).

Magnification: $\times 23,600$.

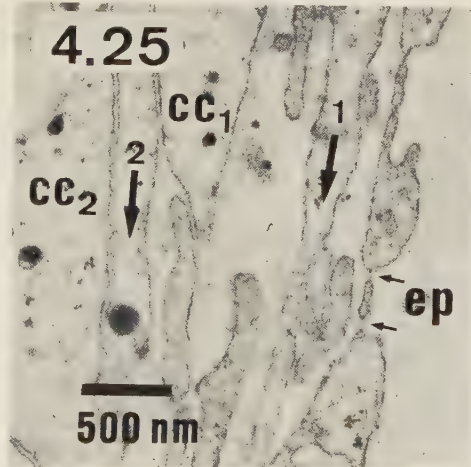
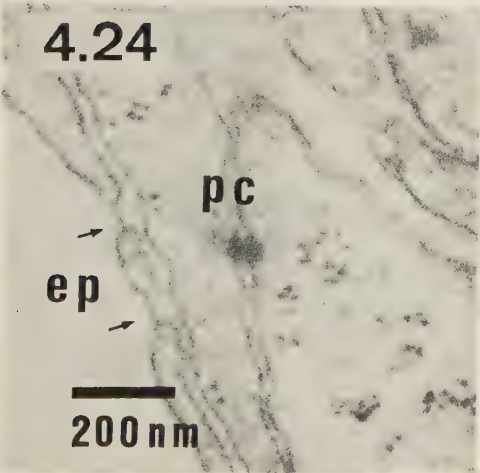
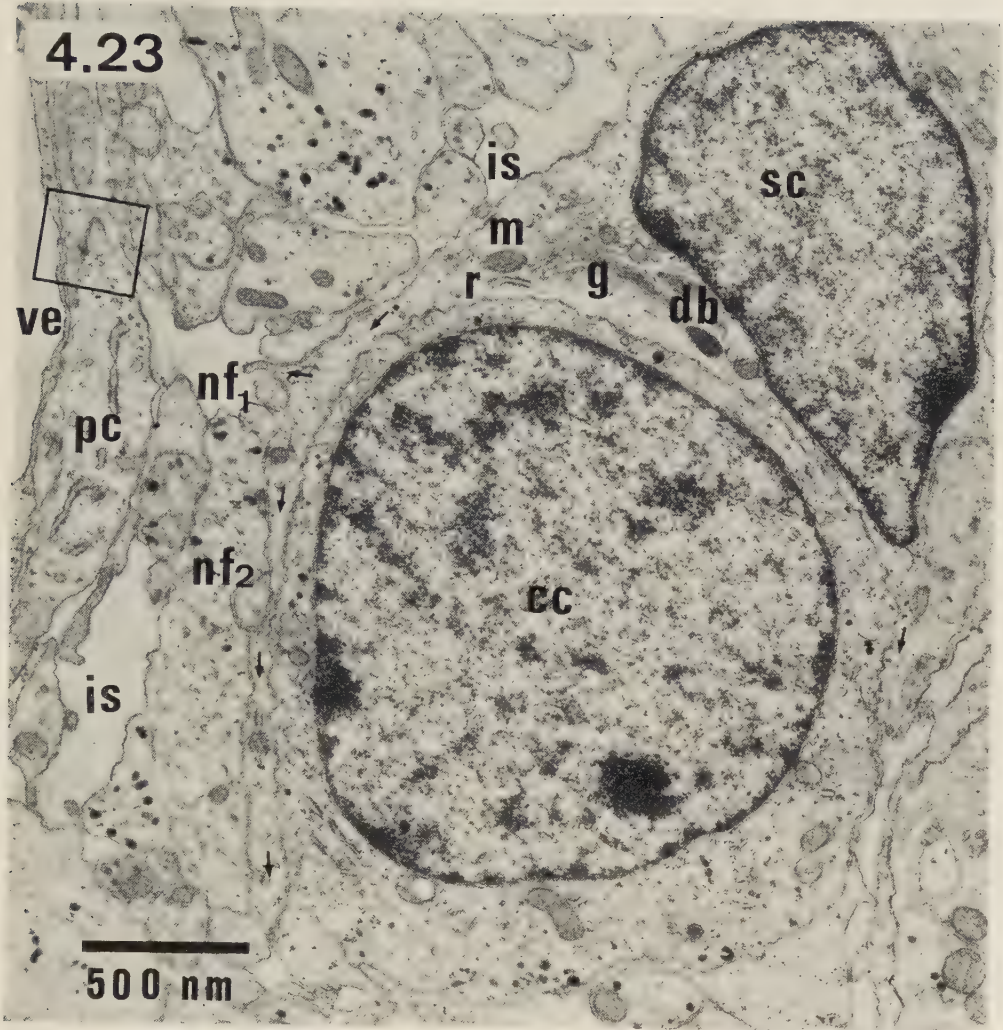


Fig. 4.26.

Golgi zone in a chief cell. Middle aorticopulmonary glomus cr 59.

The architecture of the Golgi complex includes small vesicles (1), cisterns (2) whose terminal ends are distended (3), presumably as precursors of vacuoles (4), a few of which contain electron-dense material (5). Polyribosome (r), vesicle-containing body (vcb), specific granules (sg).

Magnification: $\times 108,300$.

Fig. 4.27.

Detail of chief cell. Middle aorticopulmonary glomus cr 55.

The structure ci possibly represents an obliquely cut cilium deeply invaginated in the cytoplasm. Specific granules (sg).

Magnification: $\times 78,800$.

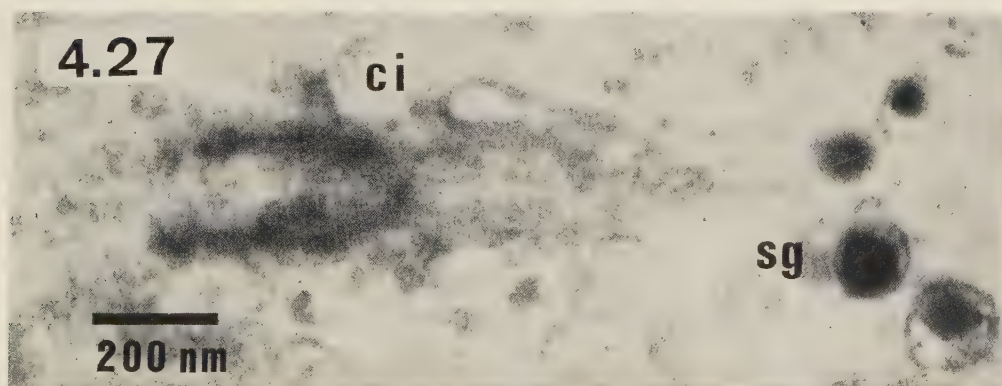
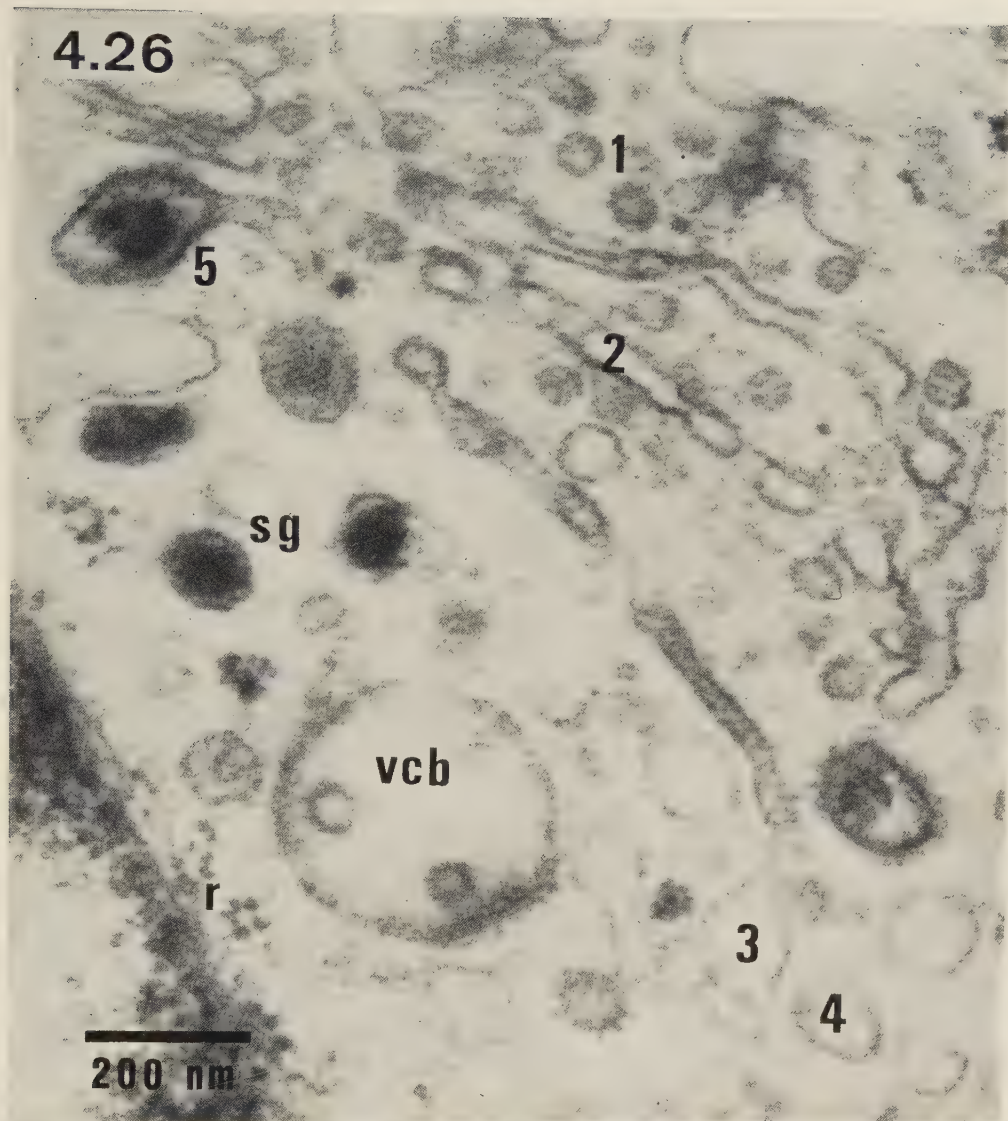


Fig. 4.28.

Detail from chief cells. Middle aorticopulmonary glomus cr 62.

The plasma membranes (cm) of the chief cells (cm) are slightly undulating and coursing parallel to an intercellular space of about 30 nm. Specific granules (sg) with membrane (sg₁), pale corona (sg₂), and electron-dense, homogeneous core (sg₃). Granular endoplasmic reticulum (ger), free ribosomes (r), agranular endoplasmic reticulum (aer), mitochondria (m), microtubules (mt).

Magnification: $\times 73,800$.

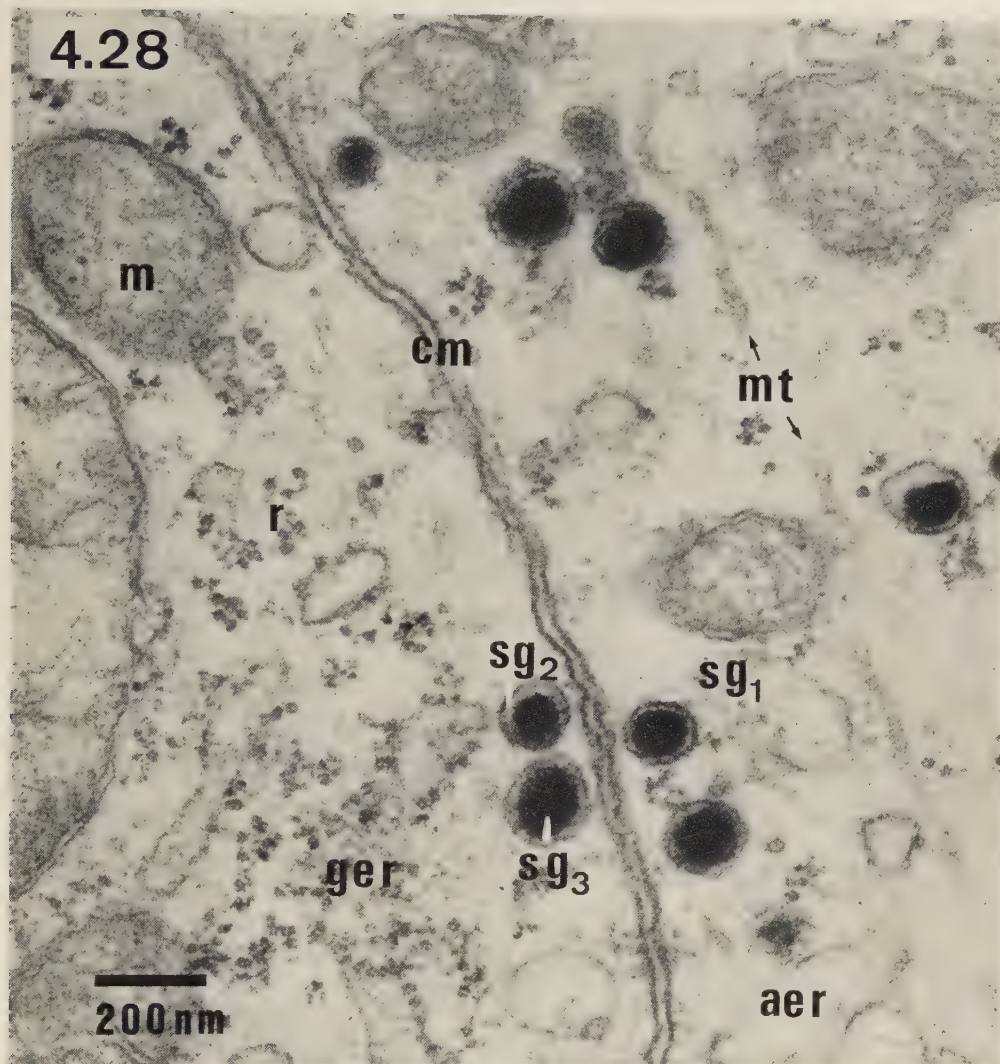
Fig. 4.29.

Detail from chief cells. Middle aorticopulmonary glomus cr 61b.

A number of desmosome-like structures (d-d) on the plasma membranes between two chief cells whose cytoplasm contains specific granules (sg).

Magnification: $\times 65,600$.

4.28



4.29

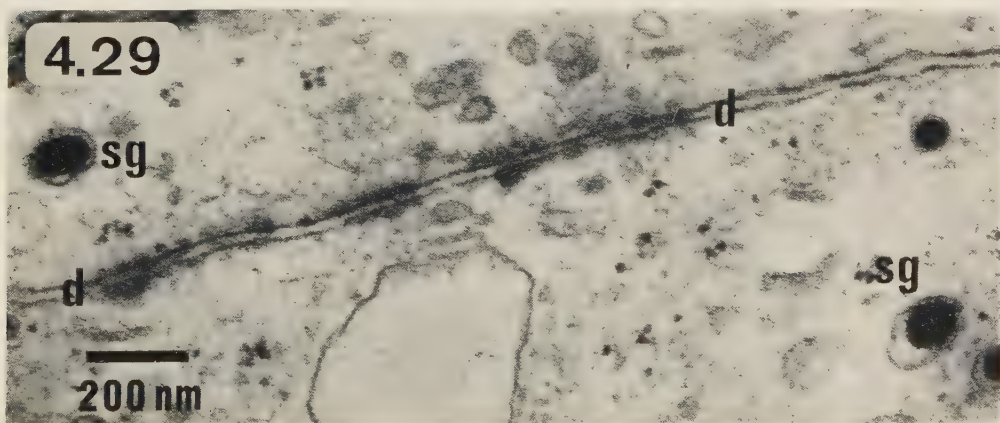


Fig. 4.30.

Light microscopic low power view. Superior aorticopulmonary glomus cr 59.

Low power view from the area of the aorticopulmonary glomus, about 80 μ m cranial to that shown in Fig. 4.18. The middle aorticopulmonary glomus (4) is included in this level, but farther posteriorly, beneath the aortic arch, immediately cranial to and to the right of the entrance of the ductus arteriosus into the aorta, there is another glomus (6), the superior aorticopulmonary glomus.

Magnification: $\times 64$.

1. Oesophagus.
2. Left main bronchus.
3. Arch of the aorta, small segment of its anterior part, cf. Fig. 4.18.
4. Middle aorticopulmonary glomus.
5. Ductus arteriosus, tangential section through the cranial adventitial – partially torn off – part of the ductus arteriosus.
6. Superior aorticopulmonary glomus.
7. Arch of the aorta, posterior part.

Fig. 4.31.

Light microscopic micrograph. Superior aorticopulmonary glomus cr 62.

The cells are grouped around vascular lumina (1) and a bundle of nerve fibres (2).

Magnification: $\times 640$.

1. Vessel.
2. Nerve fibres with Schwann cells.
3. Pericyte.
4. Chief cells.
5. Supporting cells.

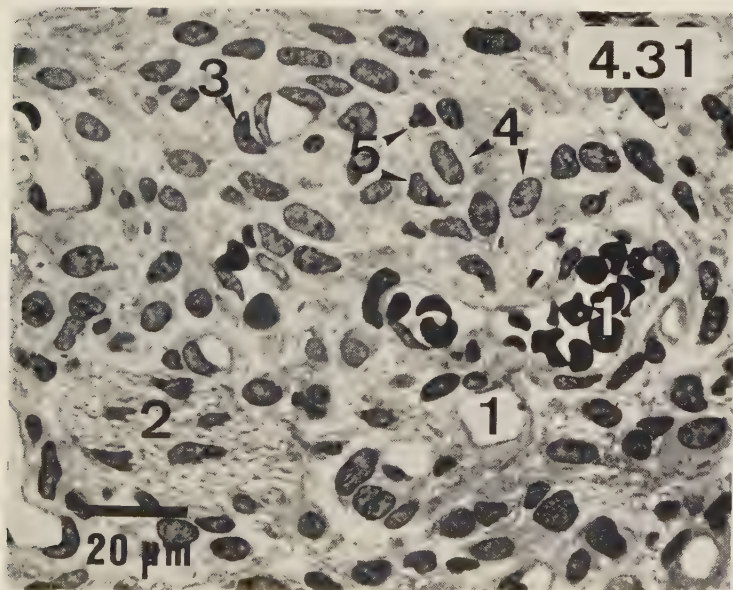
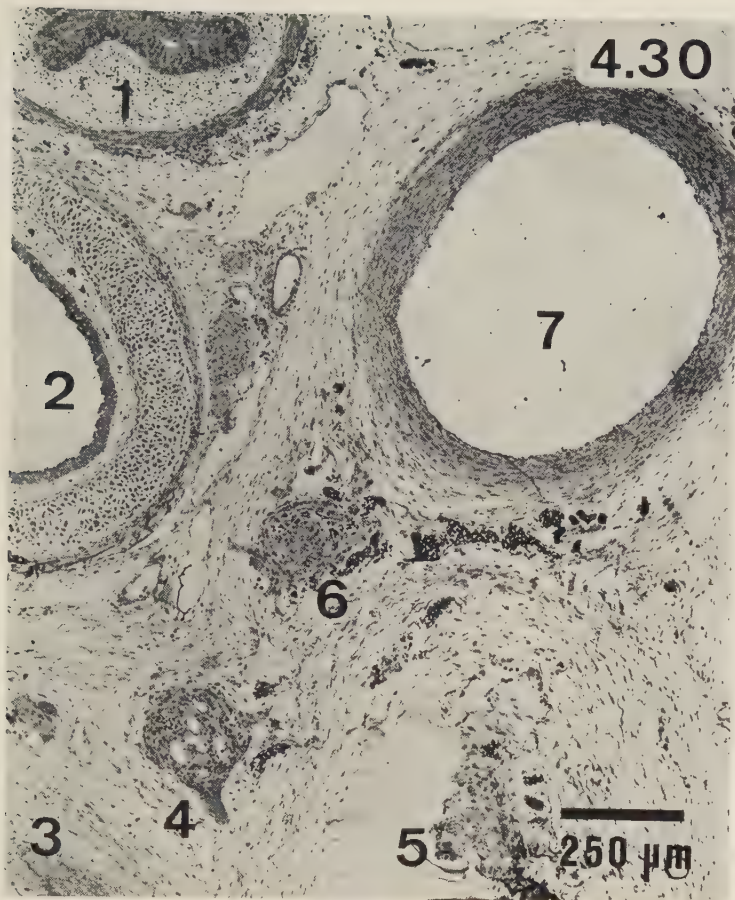


Fig. 4.32.

Electron microscopic low power view. Superior aortcopulmonary glomus cr 59.

Judging by sections cut through the nucleus the nuclei of the granular chief cells (cc_1 , cc_2 , cc_3) are rod-shaped, whereas the nuclei of the supporting cells (sc) are of a more irregular shape, adapted to the surrounding structures. The chief cells are spindle-shaped, possibly with secondary processes (cf. Fig. 4.37). The cytoplasm of the supporting cells forms bowl-shaped cups for the chief cells (arrows). Only small areas on the photomicrograph constitute irregular, extracellular interstices (is).

Magnification: $\times 4,100$.

4.32

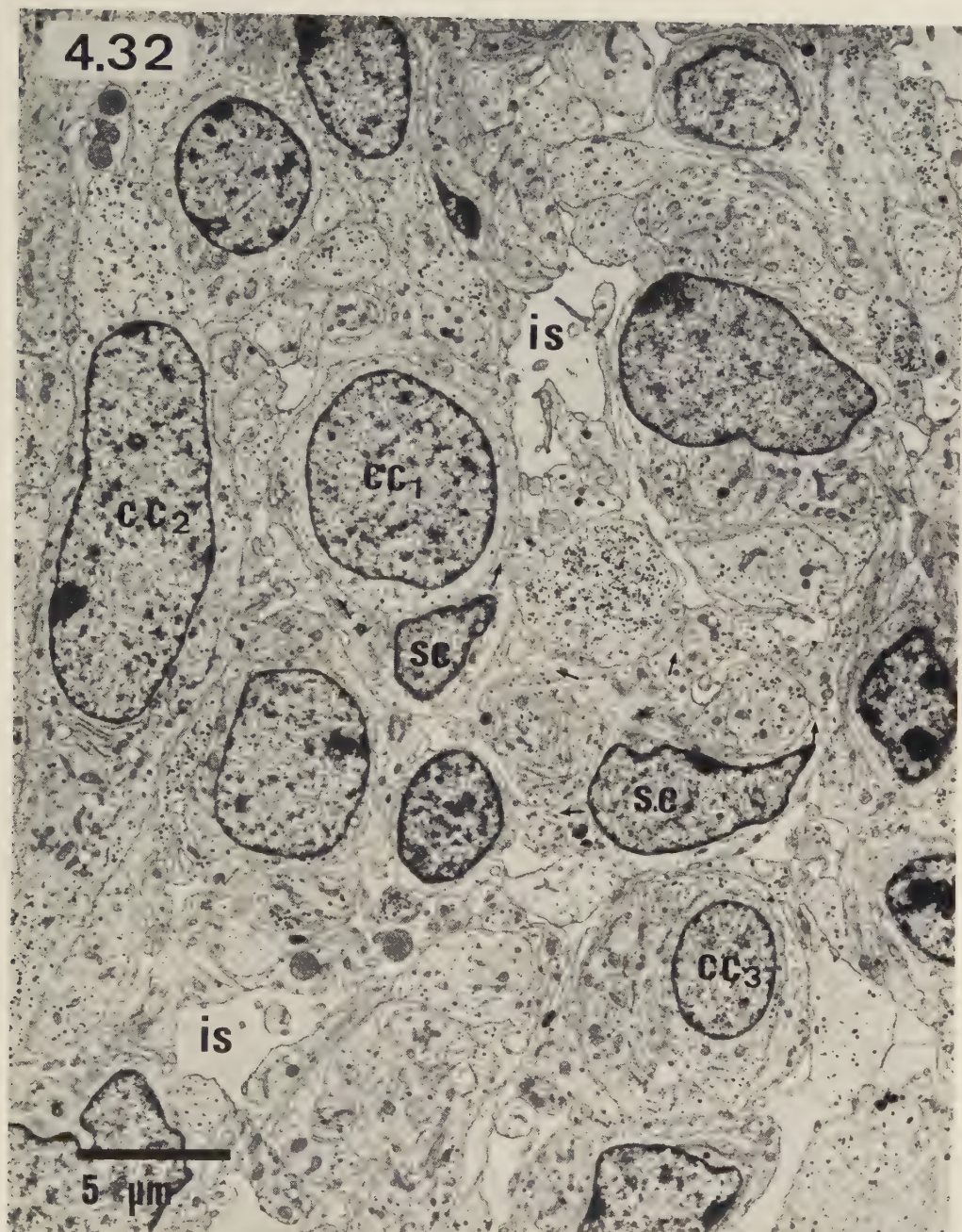


Fig. 4.33.

Relationship between chief and supporting cells. Superior aorticopulmonary glomus cr 61.

Two supporting cells (sc) are investing by their processes a group of chief cells (cc) and nerve fibres (nf). The structure marked 1 is magnified in Fig. 4.40.

Magnification: $\times 5,100$.

Fig. 4.34

Chief cells. Superior aorticopulmonary glomus cr 55.

The cytoplasm appears darker in the chief cell cut through the nucleus (cc₁) than in that which is not (cc₂). It is difficult to decide whether the different electron opacity is due solely to the larger number of ribosomes in the cell cut through the nucleus or whether it is due also to a difference in the density of the cytoplasmic ground substance. Where the cytoplasm (at the arrow) narrows there appear thin filaments reminiscent of the structures in longitudinally cut nerve fibres (nf).

Magnification: $\times 7,800$.

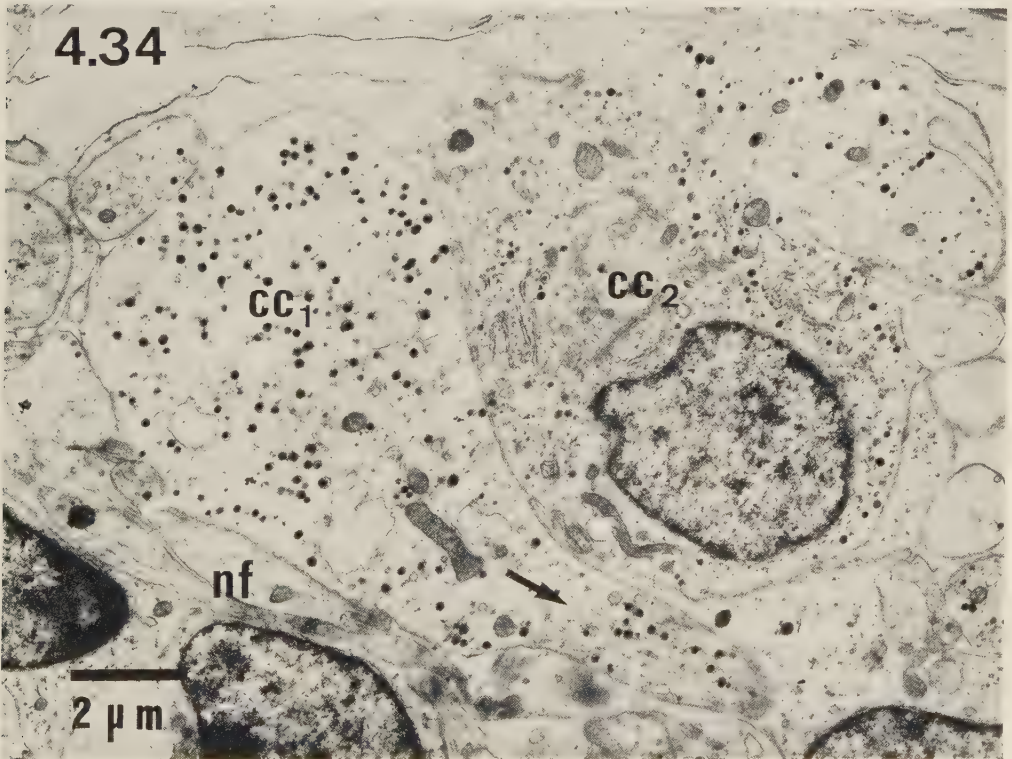
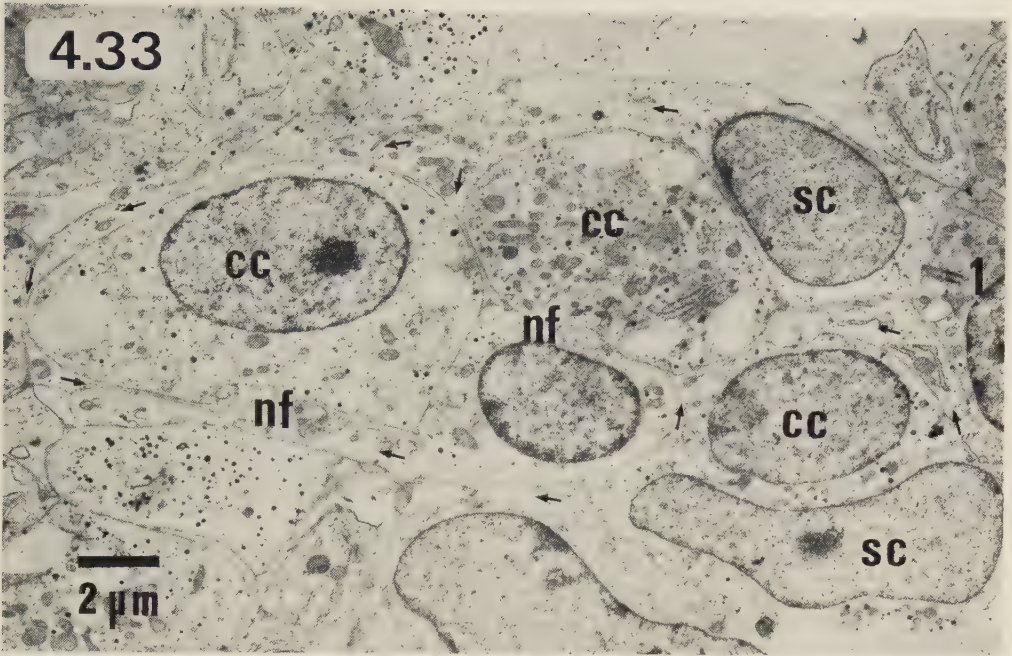


Fig. 4.35

Supporting cell. Superior aorticopulmonary glomus cr 59.

In the cytoplasm of the supporting cell (sc) membrane-bound and free ribosomes (r), small mitochondria (m), Golgi zone (g), and lysosome-like bodies (lb). The processes of the cell (arrows) are ensheating a chief cell (cc).

Magnification: $\times 11,200$.

Fig. 4.36.

Organelles in a chief cell. Superior aorticopulmonary glomus cr 55.

In the juxtannuclear area of the cytoplasm (nu) a Golgi apparatus (g), mitochondria (m), free ribosomes, mainly in the form of polyribosomes (r), granular endoplasmic reticulum (ger), a multivesicular body (vcb), osmiophilic granules (sg), a few microtubules (mt), and pale vacuoles some of which (va_1) may be Golgi vacuoles, whereas others (va_2) have possibly originated in the endoplasmic reticulum and thus represent an agranular form of the latter.

Magnification: $\times 28,600$.

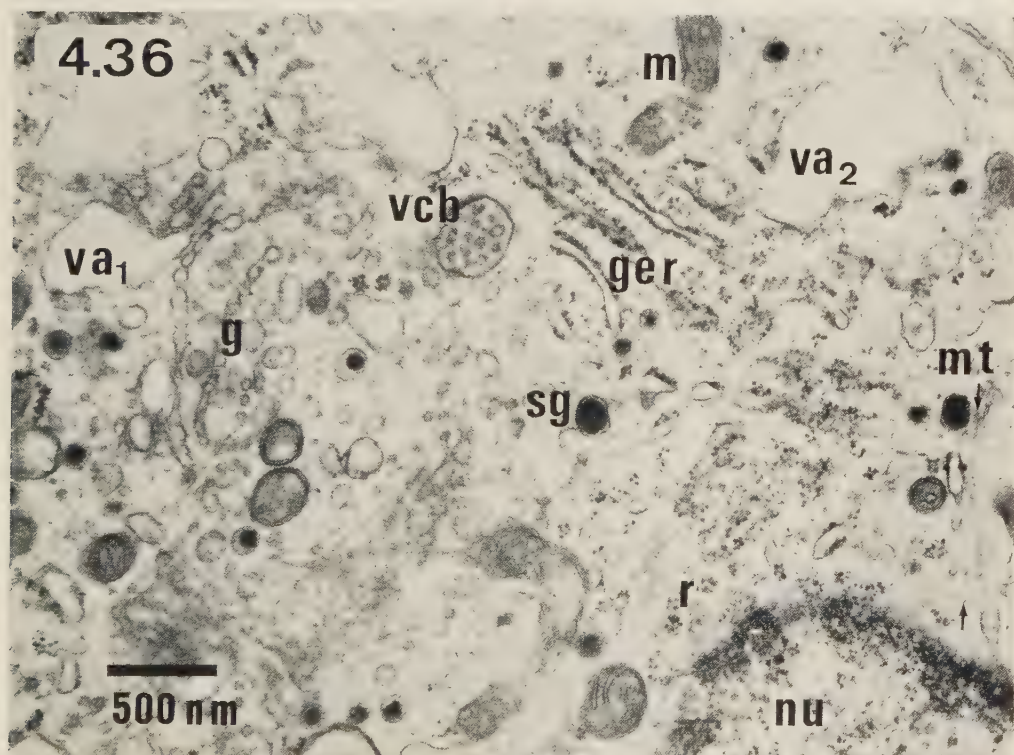
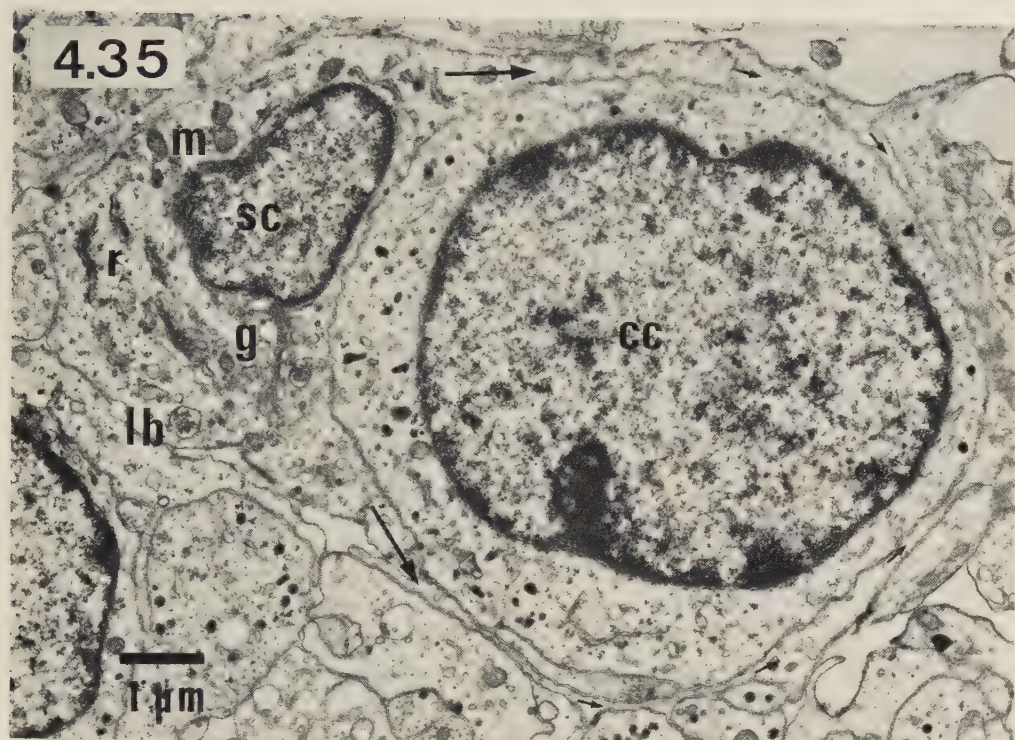


Fig. 4.37.

Chief cell extension. Superior aorticopulmonary glomus cr 55.

From the cytoplasm around the chief cell nucleus with nucleoli (nl) a long process (pcc) issues, giving off secondary processes (arrow). In the process an ample content of organelles. In particular, it will be noticed that the specific granules – though unevenly distributed – occur throughout the course. The plasma membrane of the process adjoins the interstice only in minor areas. The greater part of the surface is covered with cell parts which cannot be definitely identified.

Magnification: $\times 7,100$.

Fig. 4.38.

Contact between chief cell and nerve fibres. Superior aorticopulmonary glomus cr 59.

Part of chief cell (cc), nerve fibres (nf).

Magnification: $\times 57,000$.

Fig. 4.39

Adjoining chief cells. Superior aorticopulmonary glomus cr 55.

In a short area (d) submembranous condensation of the cytoplasmic ground substance. Specific granules (sg).

Magnification: $\times 72,000$.

Fig. 4.40.

Cilium. Superior aorticopulmonary glomus cr 61.

Basal part of a cilium (ci), presumably arising from a chief cell, cf. Fig. 4.33. Supporting cell (sc).

Magnification: $\times 51,300$.

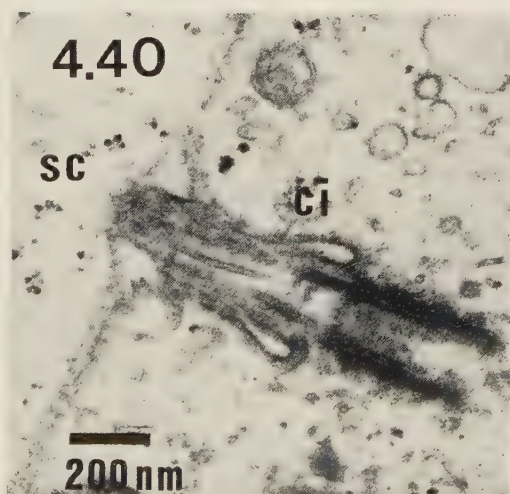
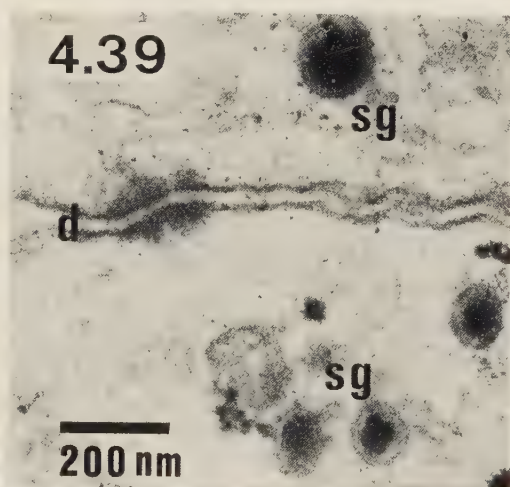
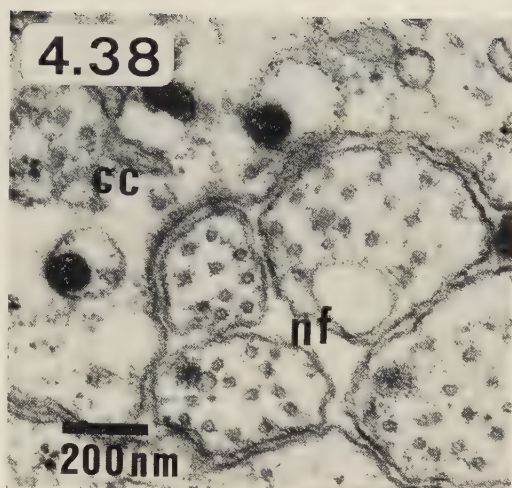
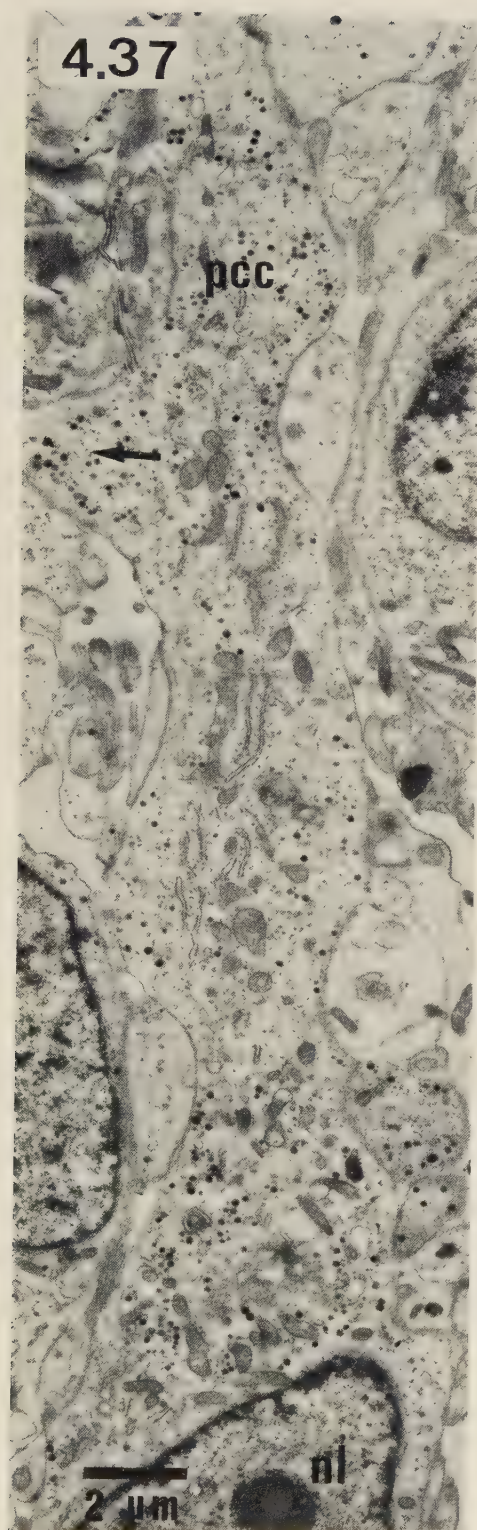


Fig. 4.41.

Vessel. Superior aorticopulmonary glomus cr 59.

In a limited area (asterisk) immediate communication between the chief cell (cc) and the vessel (ve) whose endothelium is partly covered by a pericyte (pc). The area between the arrow is further magnified in Fig. 4.42.

Magnification: $\times$ 6,800.

Fig. 4.42.

Endothelial fenestration. Superior aorticopulmonary glomus cr 59.

Magnification of an area from Fig. 4.41, showing endothelial pores (arrow), mitochondria in a pericyte process (pc), a chief cell (cc), and unidentified cell processes (asterisks).

Magnification: $\times$ 68,400.

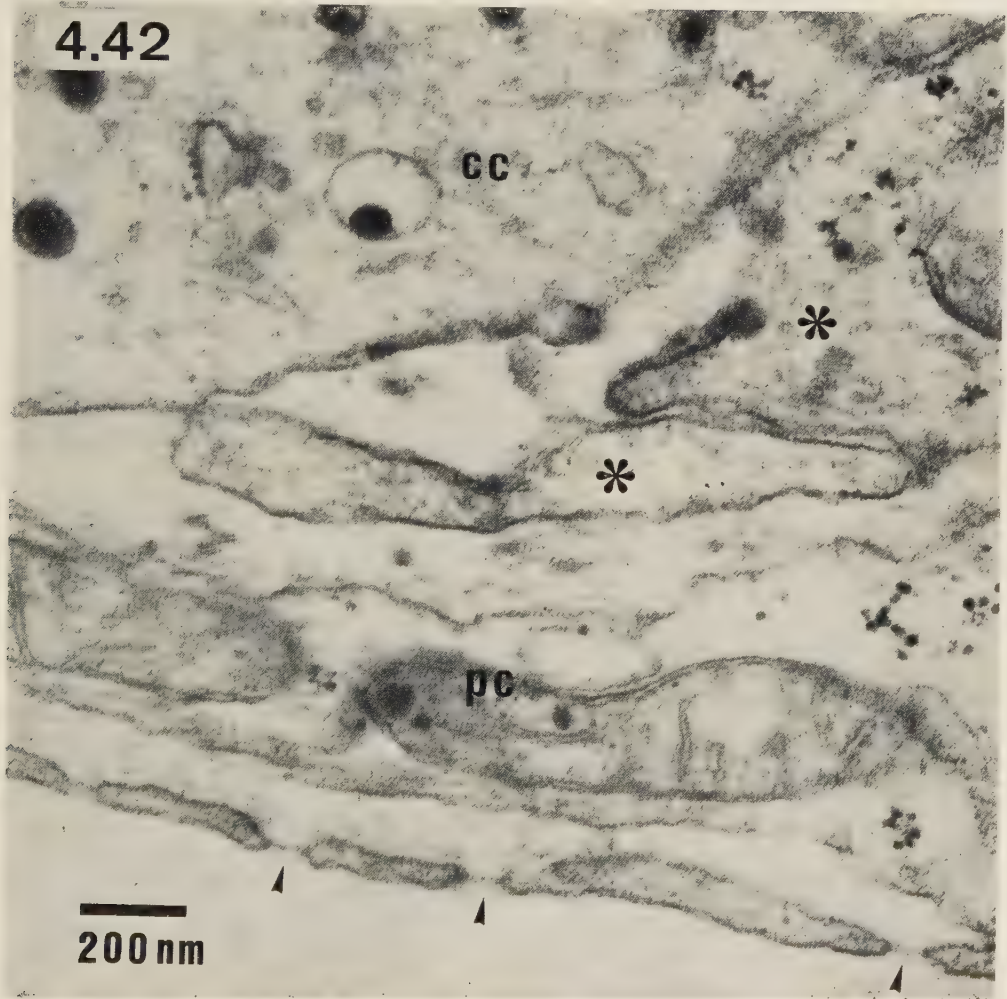
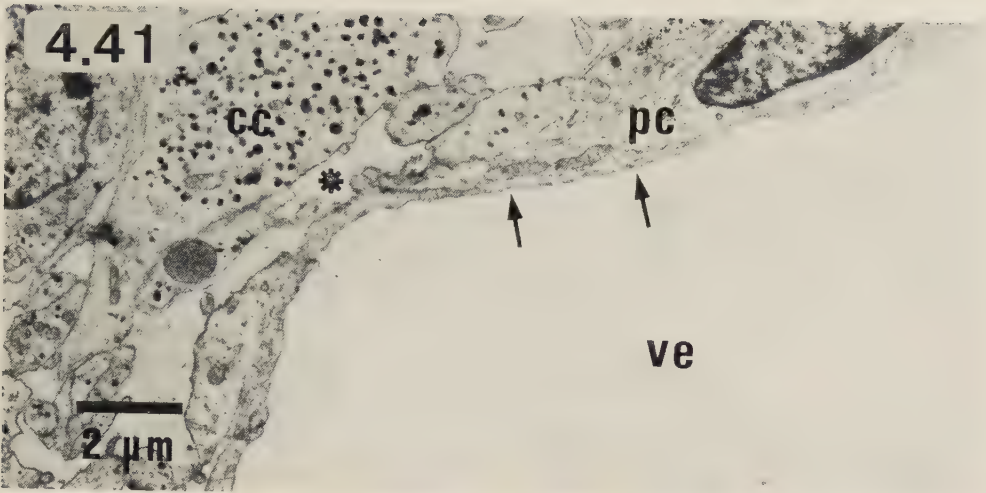


Fig. 4.43.

Golgi zone in a chief cell. Superior aorticopulmonary glomus cr 61.

In a Golgi cistern (arrows) accumulation of an electron-dense material (g), whereby arises a structure which, when disregarding the luminal connection to the Golgi cistern, resembles a specific granule (sg). Mitochondrion (m).

Magnification: $\times 74,100$.

Fig. 4.44.

Area of chief cell extension. Superior aorticopulmonary glomus cr 55.

Lysosome-like body with laminar structure (lb), specific granules (sg), obliquely cut microtubules (mt).

Magnification: $\times 62,400$.

Fig. 4.45.

Detail of chief cell. Superior aorticopulmonary glomus cr 62.

Accumulation of specific granules (sg_{1-5}) showing the variation of the granules in size, shape, and fine structure. The somewhat larger, electron-opaque body (db) and the multivesicular membrane-bounded body (vcb) presumably represent lysosomes. Free ribosomes (r).

Magnification: $\times 74,100$.

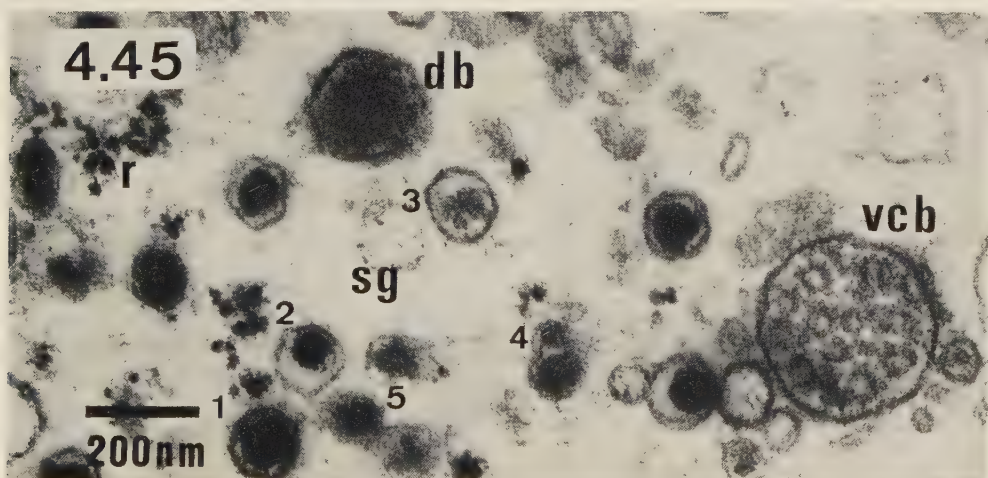
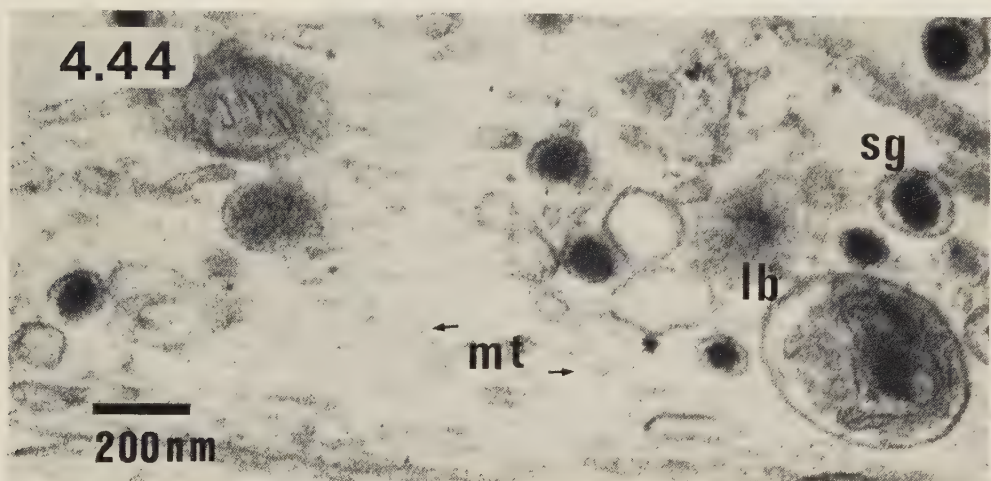
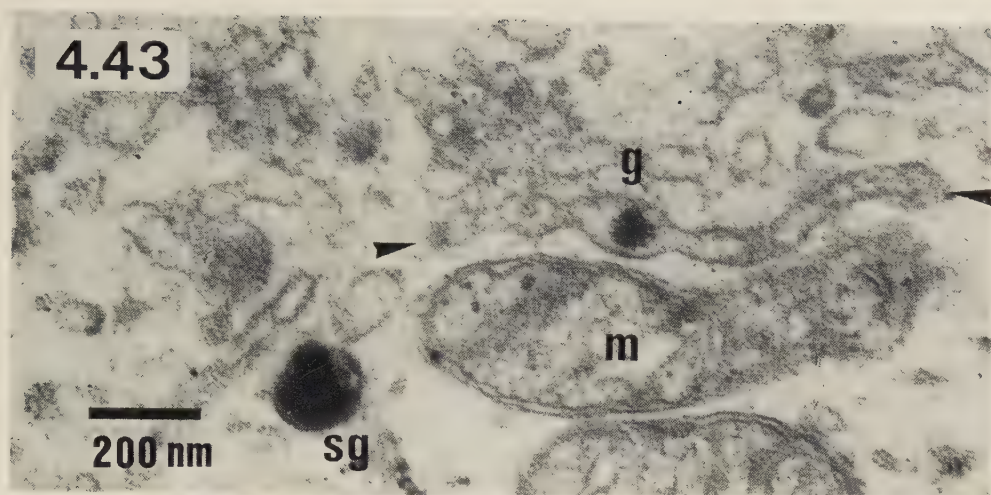


Fig. 5.1.

Example of specimen representing the area of the left subclavian glomus. Foetus cr 61.

The specimen comprises the aortic arch (1) cranial to the most proximal point of the lower concavity of the aortic arch, the commencements of the brachiocephalic trunk (2), left common carotid artery (3), left subclavian artery (5), and left vagus nerve (4), cf. Fig. 2.1. The left phrenic nerve has been removed. The photograph was taken by transillumination of the specimen while it was imbibed with liquid epoxy resin. It was embedded so that the direction of sectioning was parallel to an (approximated) sagittal plane through the aortic arch.

Magnification: ca. $\times 30$.

1. Aortic arch.
2. Brachiocephalic trunk.
3. Left common carotid artery.
4. Left vagus nerve.
5. Left subclavian artery.

Fig. 5.2.

Light microscopic low power view. Left subclavian glomus cr 62c.

Longitudinal section through the left vagus nerve (1), cf. Fig. 5.1, on a level with the most cranial part of the aortic arch whose periadventitial connective tissue (3) is visible in the bottom left-hand corner. The glomus (2) is situated in the mesenchyme between the left vagus nerve and the arch of the aorta.

Magnification: $\times 160$.

1. Left vagus nerve.
2. Glomus.
3. Aortic arch, periadventitial connective tissue sectioned tangentially.

Fig. 5.3.

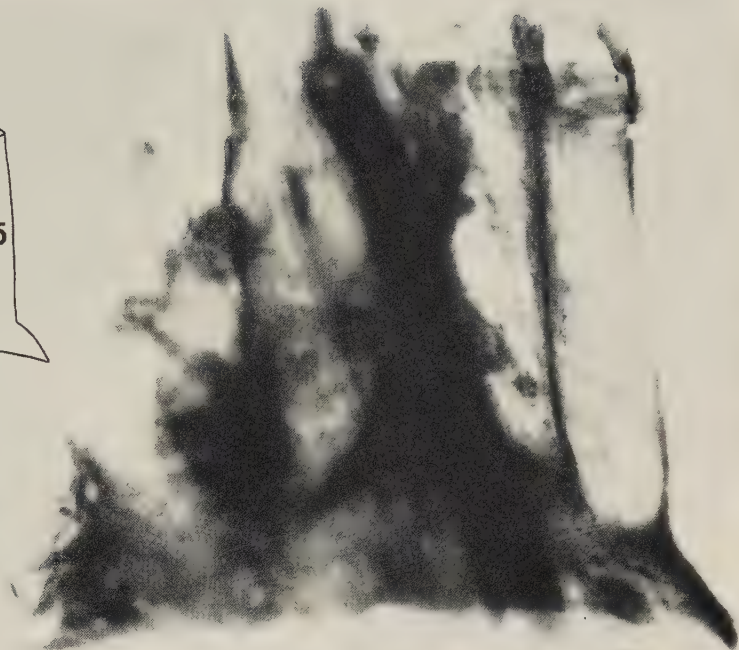
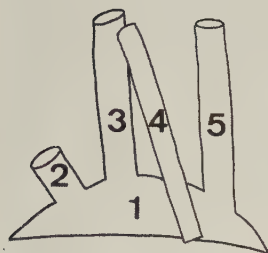
Light microscopic micrograph. Left subclavian glomus cr 62c.

This section is 10 μm deeper than the section depicted in Fig. 5.2. The glomus (1) is situated beside a vertical nerve (3) and is surrounded by thin-walled vessels (2).

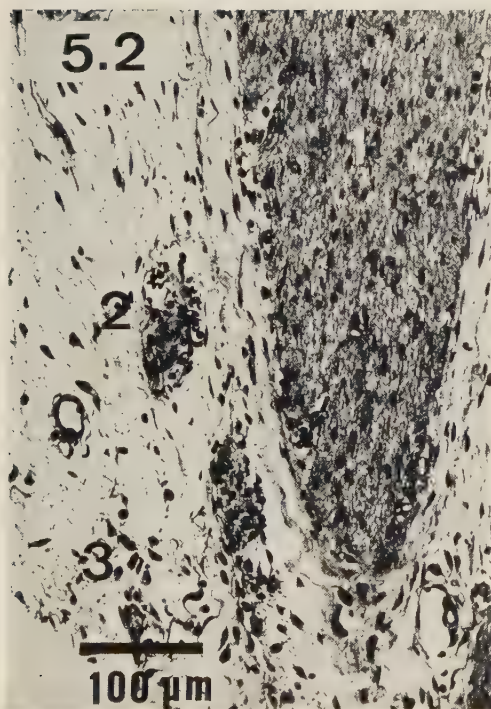
Magnification: $\times 640$.

1. Glomus.
2. Vessels.
3. Nerve.

5.1



5.2



5.3

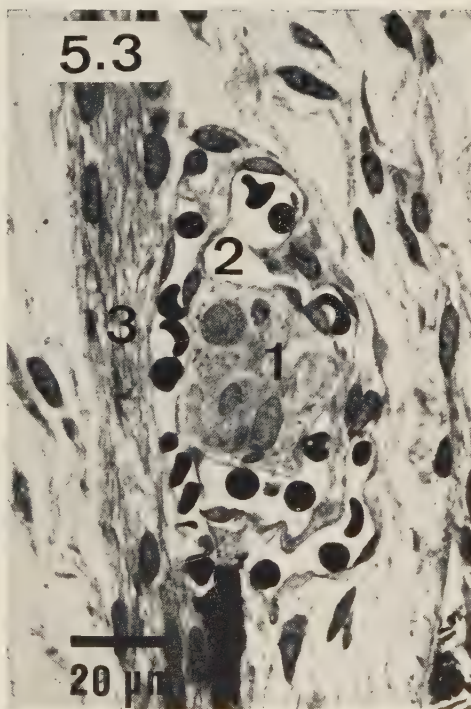


Fig. 5.4.

Light microscopic low power view. Left subclavian glomus cr 59a.

Example of a left subclavian glomus found in the specimen comprising the area of the aorticopulmonary glomus from foetus cr 59. The section is about 200 μ m cranial to that shown in Fig. 4.30 and runs through the posterior part of the aortic arch (7). On the left surface of the arch the left vagus nerve (6) and the left recurrent laryngeal nerve (5). The latter appears again on the right (3) between the trachea (2) and oesophagus (1). The glomus (4) is situated in the connective tissue on the left surface of the aortic arch, about $\frac{3}{4}$ mm anterior to the left vagus nerve.

Magnification: $\times 64$.

1. Oesophagus.
2. Posterior tracheal wall.
3. Left recurrent laryngeal nerve after having curved around the ductus arteriosus.
4. Left subclavian glomus.
5. Left recurrent laryngeal nerve, just after having separated from the left vagus nerve.
6. Left vagus nerve.
7. Arch of aorta, posterior part.
8. The small prominence into the vascular lumen marks the origin of the left subclavian artery.

Fig. 5.5.

Light microscopic micrograph. Left subclavian glomus cr 62b.

The glomus cells, among which only a vague distinction can be made between chief cells (1) and supporting cells (2), form incomplete whorls between the vascular lumina (3).

Magnification: $\times 640$.

1. Chief cells.
2. Supporting cells.
3. Vascular lumina.

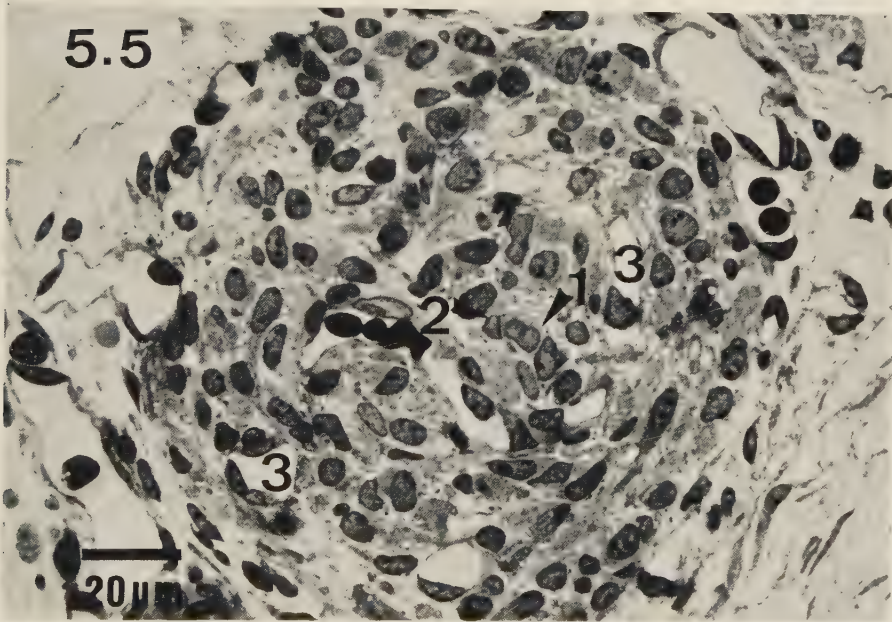
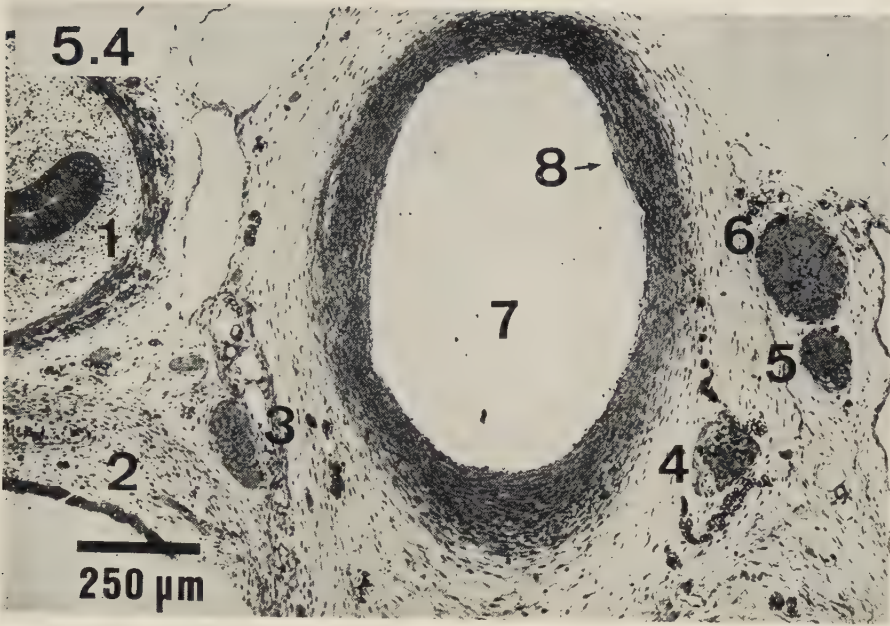


Fig. 5.6.

Electron microscopic low power view. Left subclavian glomus cr 62a.

By the nuclear shape and the cytoplasmic content of osmiophilic granules, chief cells (cc) can be distinguished from supporting cells (sc). A few cells (asterisk) cannot be identified. Chief-cell processes (pcc), vessels (ve), bundles of nerve fibres (nf), fibroblastic processes and collagen fibres at the surface of the glomus (cf).

Magnification: $\times 4,100$.

5.6

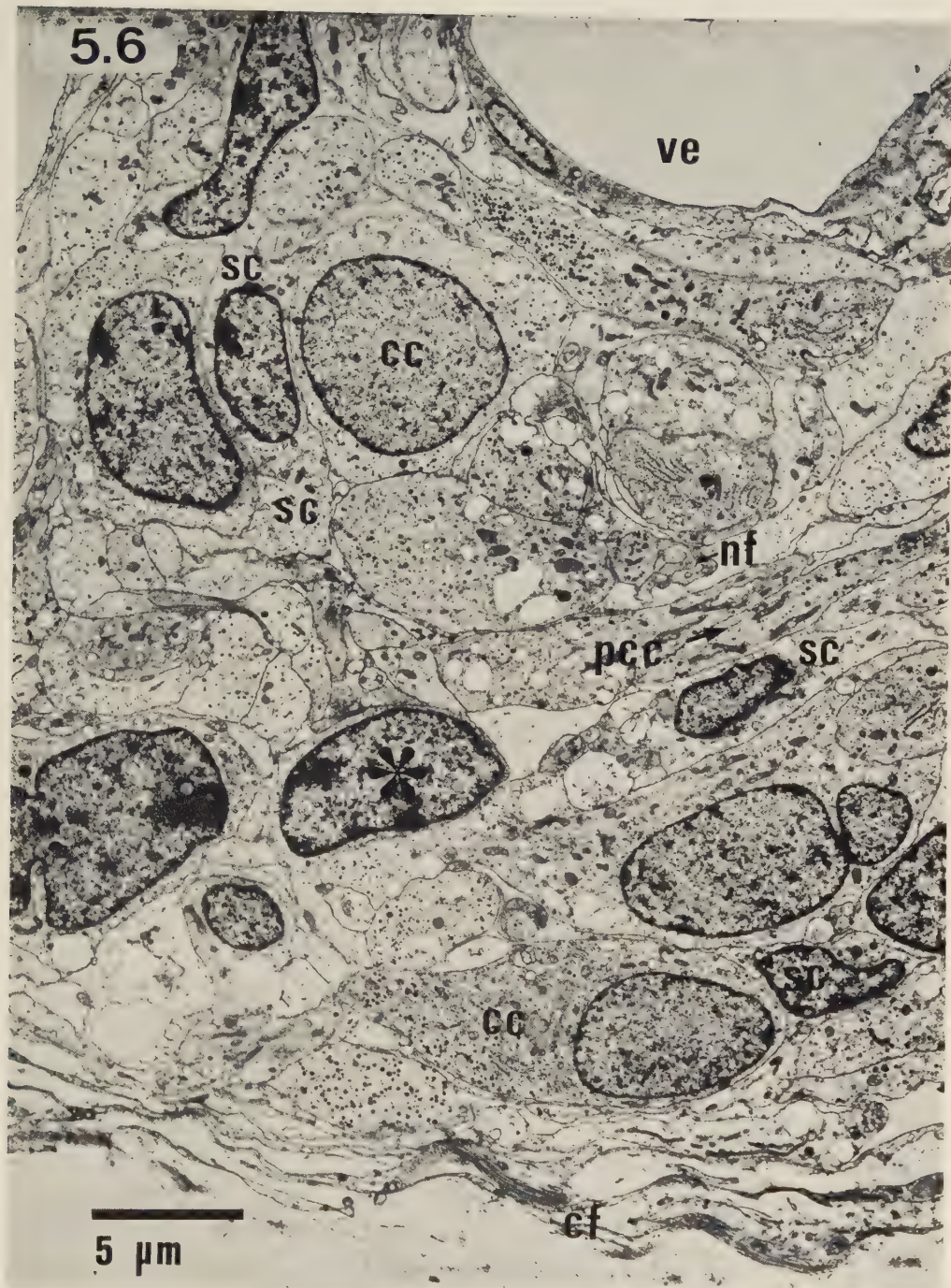


Fig. 5.7.

Supporting cell. Left subclavian glomus cr 62b.

The supporting cell (sc) invests by its processes (arrows) a chief cell (cc_1) and adjoins on the outside other chief cells (cc_2) and nerve fibres (nf). The cytoplasmic ground substance in chief cell cc_2 seems paler than that in chief cell cc_1 .

Magnification: $\times 9,500$.

Fig. 5.8.

Organelles in chief cell. Left subclavian glomus cr 55.

In the juxtanuclear cytoplasm there is int. al. granular endoplasmic reticulum (ger), Golgi zone (g), mitochondria (m), specific granules (sg), and possibly a cilium (ci). The plasma membrane is enveloped by supporting cells (sc). Between the chief and supporting cells nerve fibres (nf).

Magnification: $\times 16,500$.

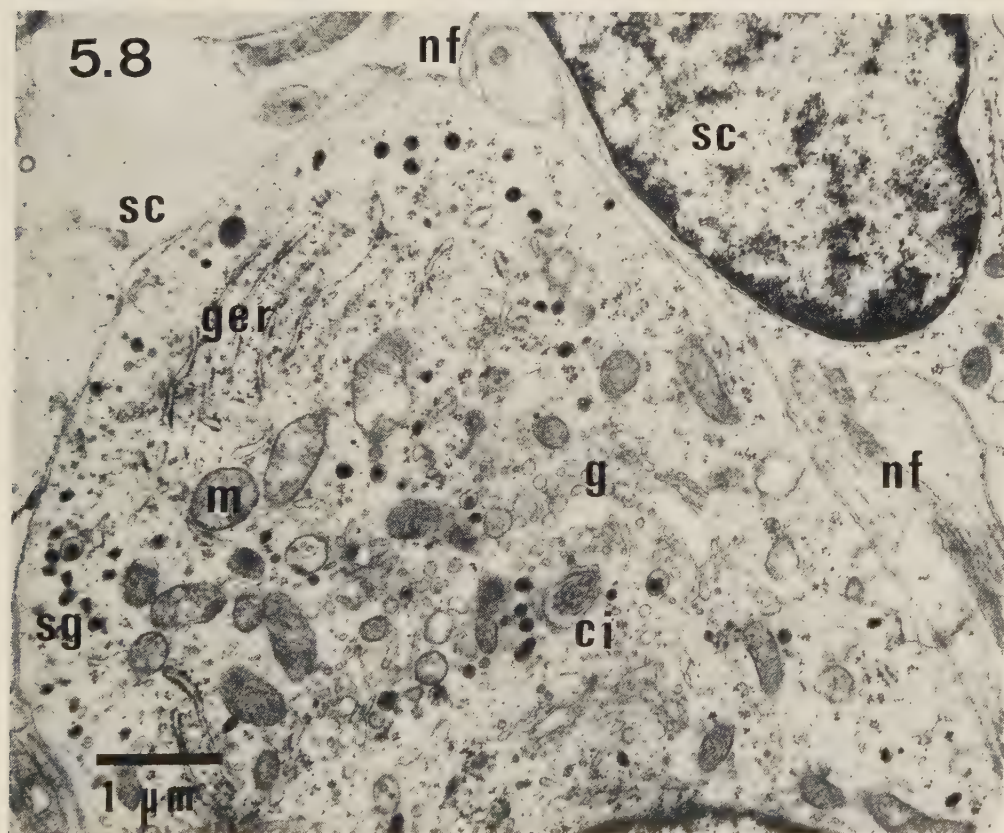
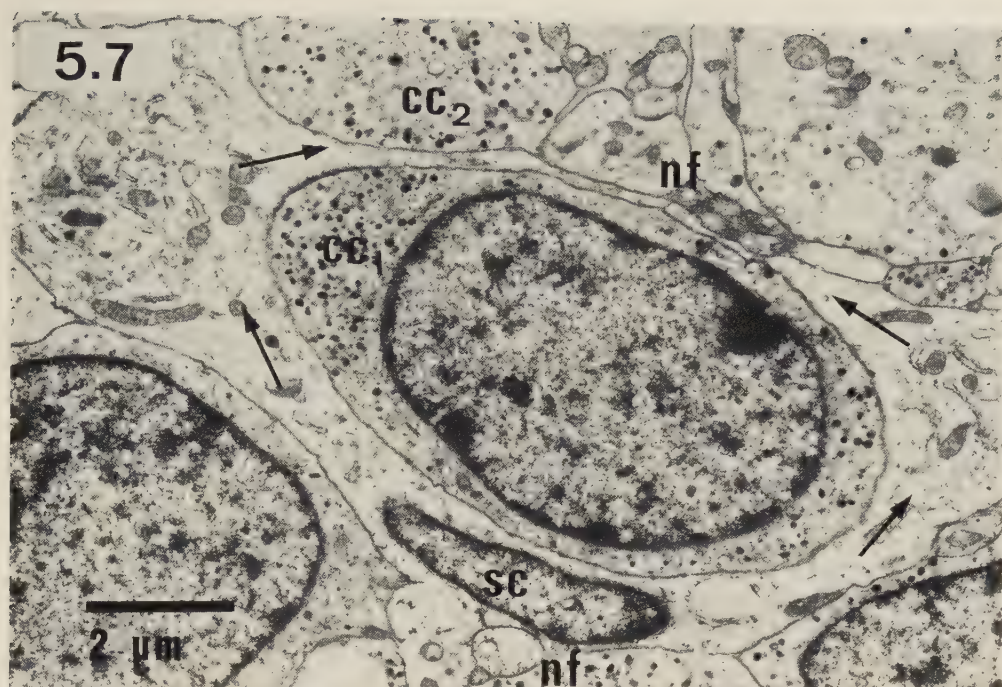


Fig. 5.9.

Vessel. Left subclavian glomus cr 61.

The vascular lumen (ve) is surrounded by endothelium (en) and a perivascular cell (pc). Around the vessel there are chief cells (cc) and supporting cells (sc). The framed area is further magnified in Fig. 5.10.

Magnification: $\times 4,800$.

Fig. 5.10.

Endothelial fenestrae. Left subclavian glomus cr 61.

Further magnification of the framed area of Fig. 5.9. which shows that between the chief cell with specific granules (sg) and the vessel with fenestrated endothelium (ep) a non-granular cell process is interposed (arrow).

Magnification: $\times 76,500$.

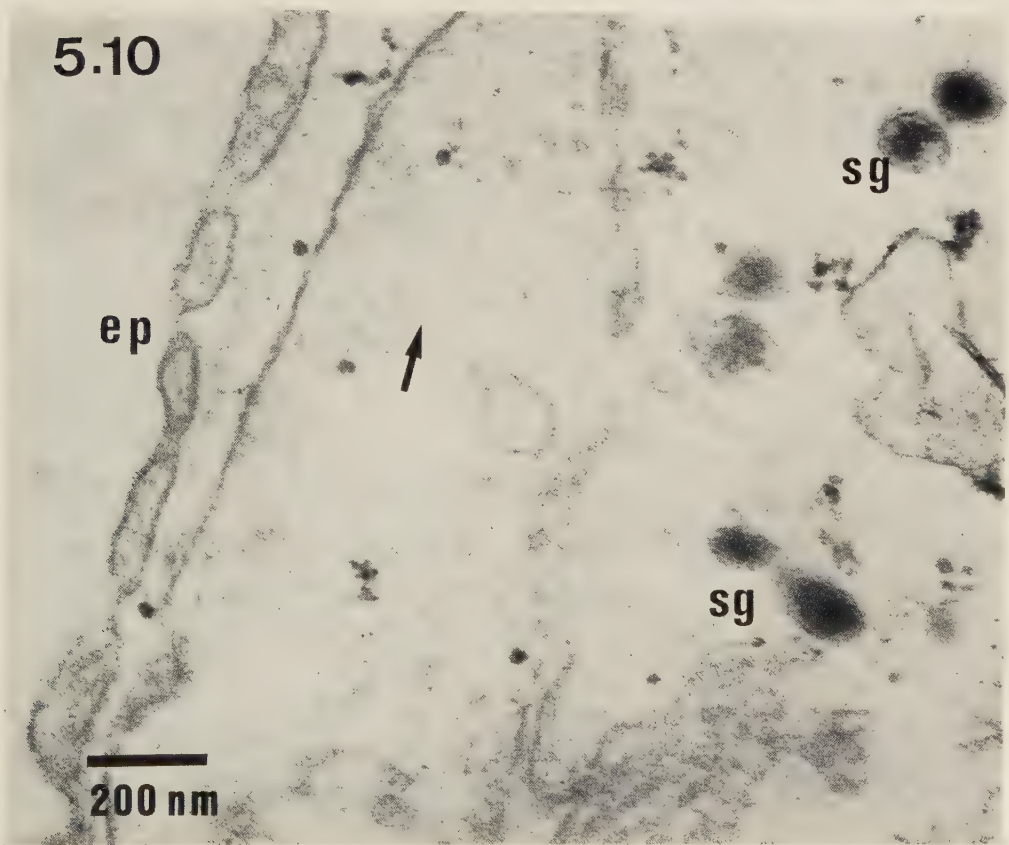
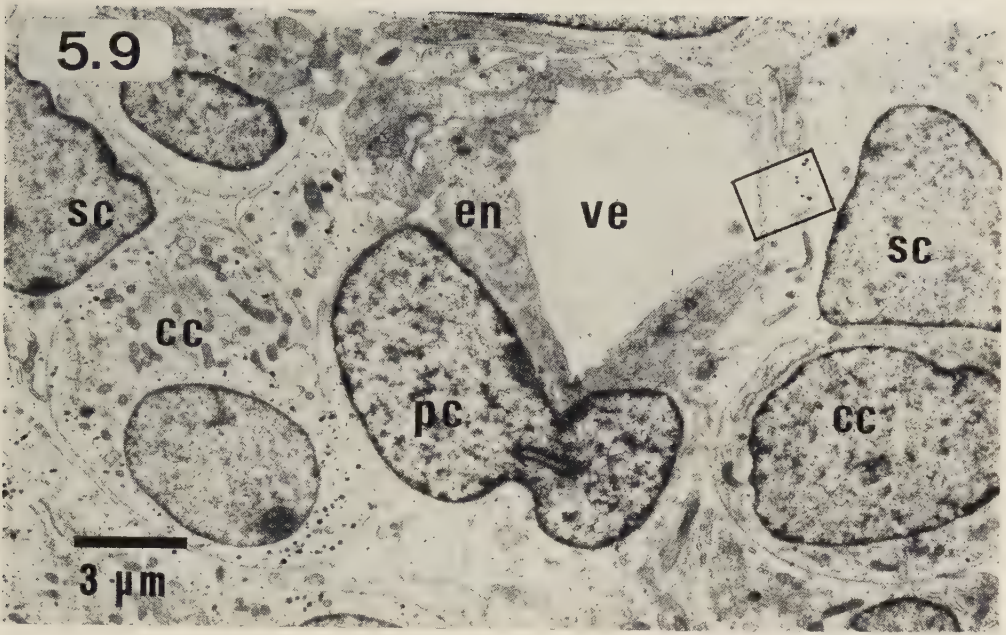


Fig. 5.11.

Area of chief cell and its relation to vessels. Left subclavian glomus cr 62c.

The perinuclear cistern of the chief cell is closed by a nuclear pore (np). In the cytoplasm several large vacuoles with pale contents (va), Golgi zone (g) (cf. Fig. 5.14), short granular cisterns and free ribosomes (r), mitochondria (m), and specific granules (sg). The cell is invested by supporting-cell processes (arrows). In the paravascular space collagen fibres (cf). The vessel contains a red blood cell (rbc), and its endothelium is fenestrated (ep).

Magnification: $\times 19,500$.

Fig. 5.12.

Organelles in chief cells. Left subclavian glomus cr 59b.

Granular endoplasmic reticulum (ger), polyribosomes (r), electron-opaque bodies (db), vesicle-containing body (vcb), mitochondria (m), specific granules (sg), desmosomes (d_1 , d_2). Nerve fibres (nf) course between the cells.

Magnification: $\times 19,500$.

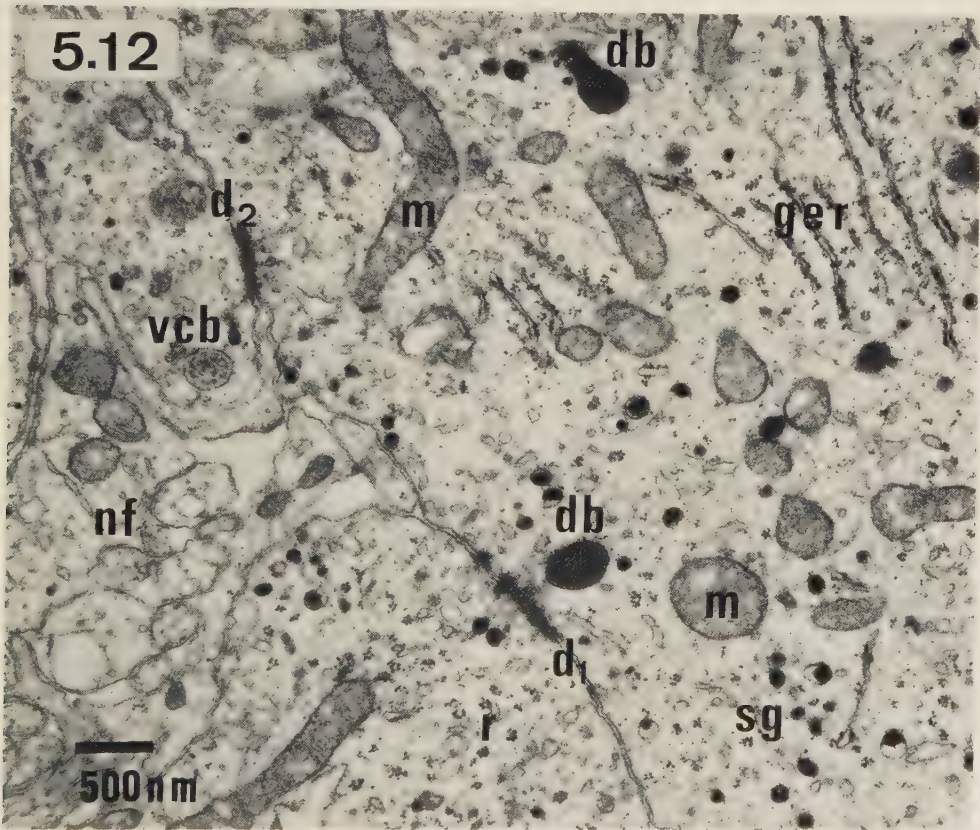
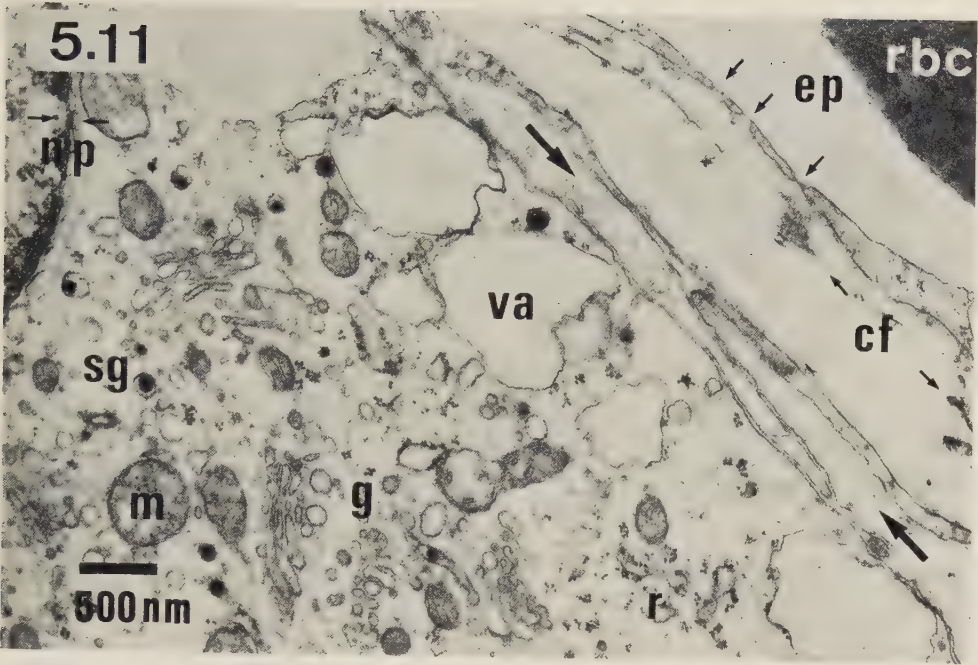


Fig. 5.13.

Detail of chief cell. Left subclavian glomus cr 59b.

Longitudinally sectioned cilium (ci) invaginated in a cell containing specific granules (sg).

Magnification: $\times 54,200$.

Fig. 5.14.

Detail of chief cell. Left subclavian glomus cr 62c.

The Golgi zone (g), cf. Fig. 5.11, consists of flat cisterns (1), vacuoles (2), and vesicles (3). One of the Golgi cisterns shows, compared with the structure in the osmiophilic granules (sg), signs of granulogenesis (arrow). Microsome (r).

Magnification: $\times 65,600$.

Fig. 5.15.

Detail of chief-cell process. Left subclavian glomus cr 62b.

Apart from specific granules (sg) there are longitudinally sectioned microtubules (mt) and agranular cisterns (aer).

Magnification: $\times 57,000$.

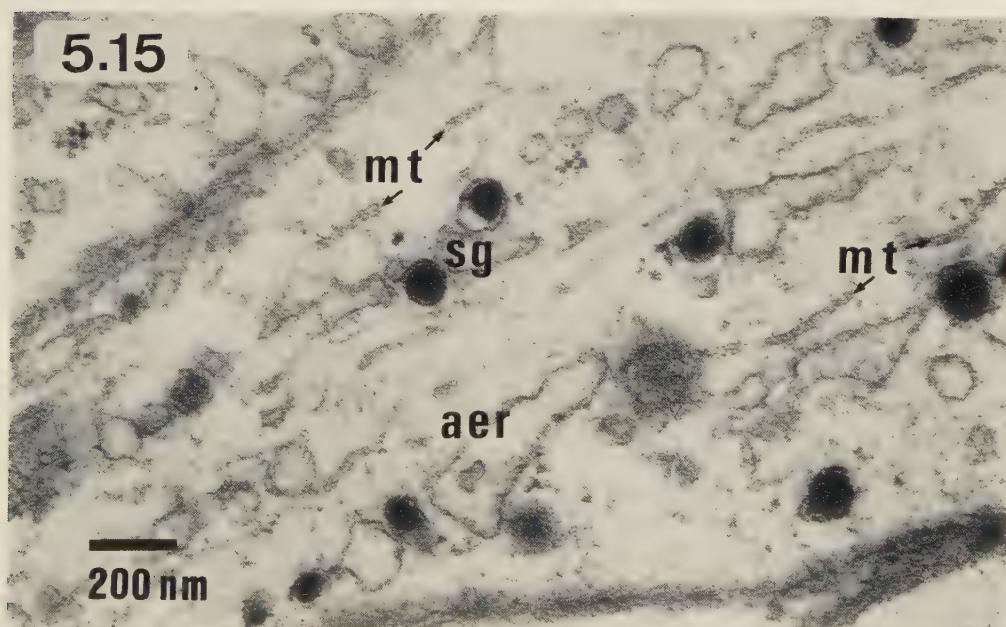
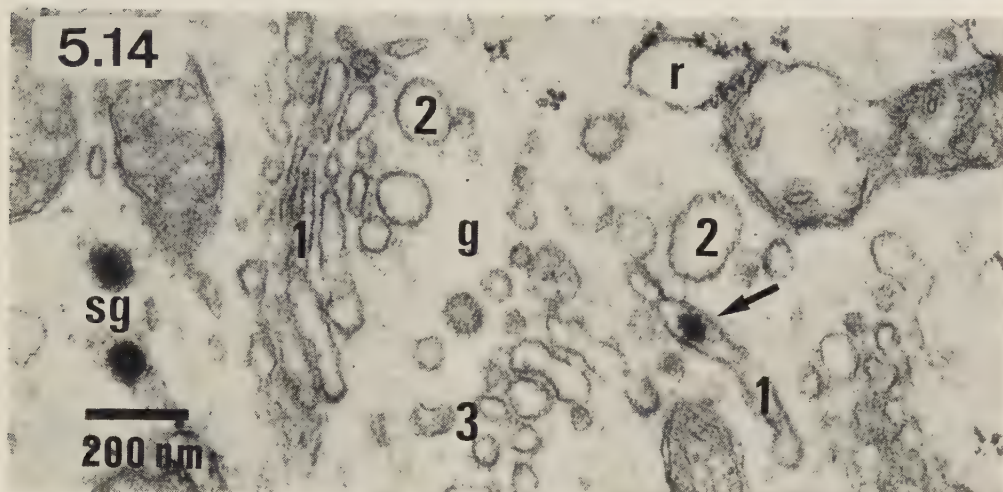
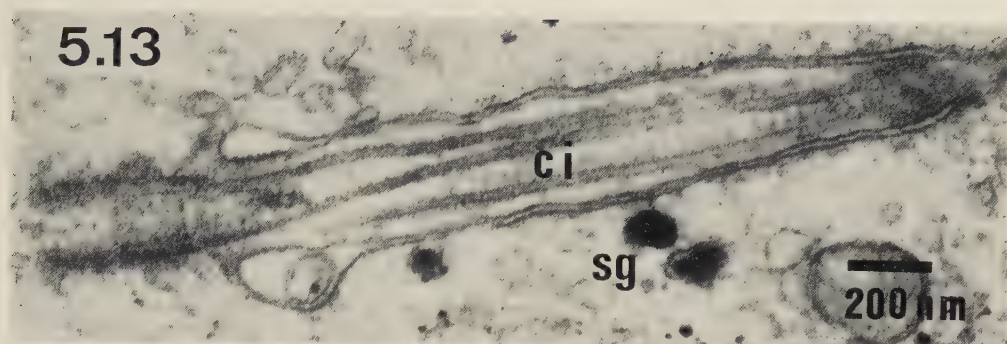


Fig. 5.16.

Nerve fibres. Left subclavian glomus cr 62b.

Transversely sectioned protoplasmic processes (1–5) reminiscent of nerve fibres in their content of tubular structures and small mitochondria (3). Two of the processes (4, 5) also contain osmiophilic granules. Therefore, they may be transversely cut chief-cell processes which (cf. Fig. 5.15) contain longitudinally sectioned microtubules. If a section through a chief-cell process has not hit a place where osmiophilic granules are present, the process cannot be distinguished from a nerve fibre (2, 3). There is no synaptic specialization between the chief cell (cc) and the axon-like processes.

Magnification: $\times 57,000$.

Fig. 5.17.

Lysosomes in chief cell. Left subclavian glomus cr 59a.

Lysosome-like bodies, one laminar (lb) and one multivesicular (vcb). Granular endoplasmic reticulum (ger).

Magnification: $\times 45,600$.

Fig. 5.18.

Detail of chief cells. Left subclavian glomus cr 55.

Transitional zone (arrow) between granular (ger) and agranular (aer) endoplasmic reticulum. Desmosome (d).

Magnification: $\times 54,200$.

Fig. 5.19.

Desmosomes between chief cells. Left subclavian glomus cr 59b.

Desmosome-like structure (d-d) with increased density of the plasma membranes and sub-membranous cytoplasmic condensation as well as preserved, pale intercellular space. Mitochondrion (m) with mitochondrial granule (arrow), electron-dense body (db), polyribosomes (r), specific, membrane-bound osmiophilic granules (sg).

Magnification: $\times 57,000$.

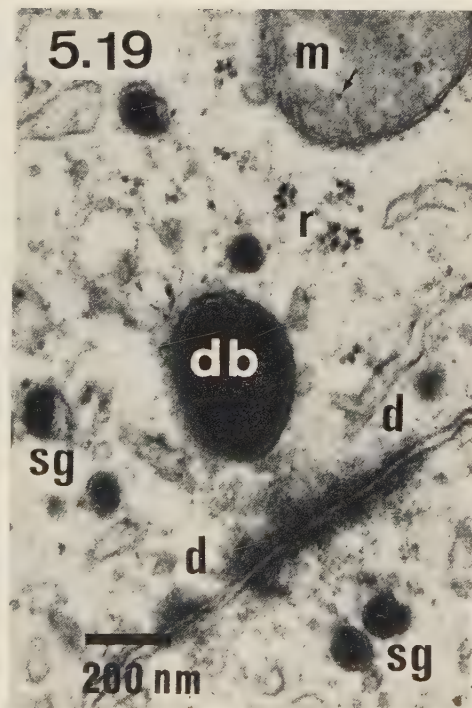
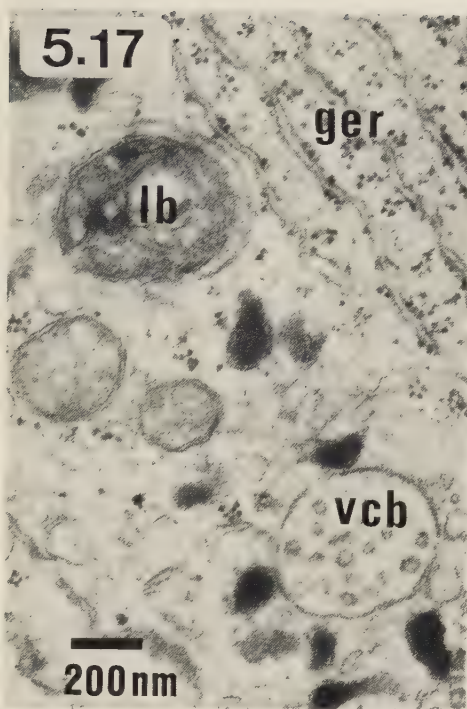
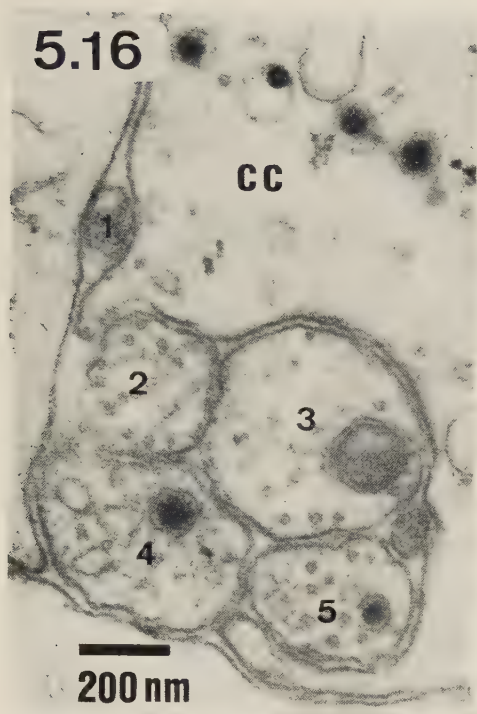


Fig. 5.20.

Example of specimen representing the area of the right subclavian glomus. Foetus cr 61.

Specimen embedded with a view to locating the right subclavian glomus. It was embedded on the flat lid of a Beem capsule and oriented in a way so that the vessels were sectioned longitudinally. The photograph was taken with transillumination of the Maraglas-imbibed preparation before polymerization of the resin.

Magnification: $\times$ ca. 20.

1. Brachiocephalic trunk.
2. Right common carotid artery.
3. Right subclavian artery.
4. Right vagus nerve.
5. Ganglion of sympathetic cervical trunk (cf. Fig. 9.6).
6. Ansa subclavia.

Fig. 5.21.

Light microscopic low power view. Right subclavian glomus cr 62.

Longitudinal section through the area of the right subclavian glomus dorsal to the vagus nerve, cf. Fig. 5.20. The glomus (4) is situated in the bifurcation of the brachiocephalic trunk (1) closer to the common carotid (2) than to the subclavian artery (3).

Magnification: $\times$ 45.

1. Brachiocephalic trunk.
2. Right common carotid artery.
3. Right subclavian artery.
4. Glomus, cf. Fig. 5.22.

Fig. 5.22.

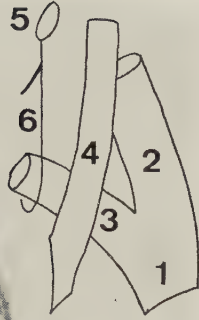
Light microscopic micrograph. Right subclavian glomus cr 62.

Magnification of the area marked 4 in Fig. 5.21. The glomus cells (1) are lying around a vessel (2) which forms a plexus at the surface of the organ where also a bundle of nerve fibres (3) is visible.

Magnification: $\times$ 640.

1. Glomus cells.
2. Vessel.
3. Nerve fibres.

5.20



5.21



5.22

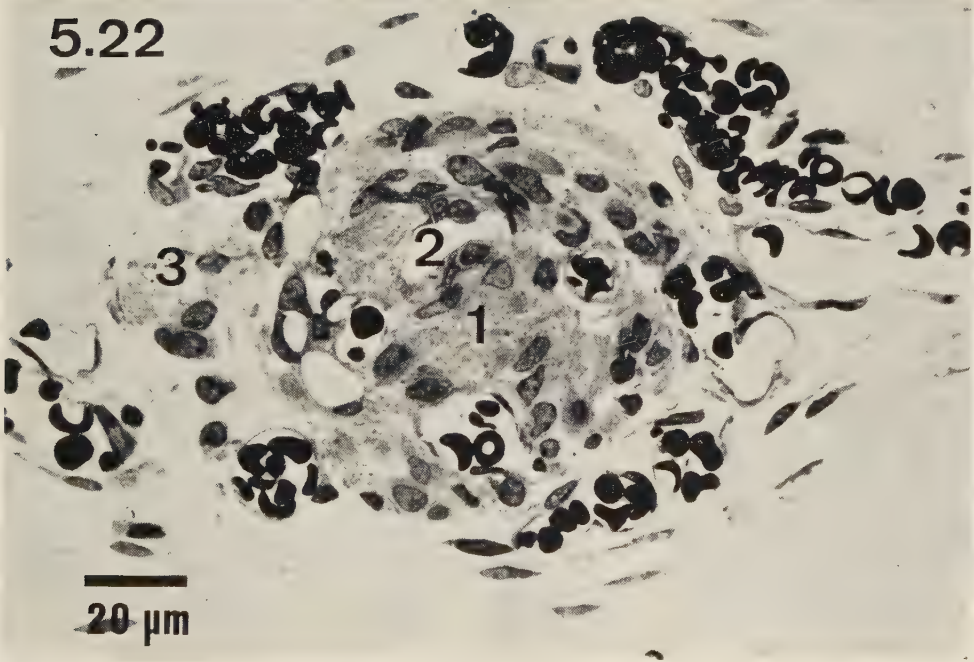


Fig. 5.23.

Electron microscopic low power view. Right subclavian glomus cr 62.

By light microscopy it is not possible to distinguish the various types among the glomus cells. Electron microscopy clearly shows that the majority of the cells, chief cells (cc), contain highly contrasting granules in their cytoplasm, whereas a few, supporting cells (sc), are agranular. The nuclei of the chief cells are usually oval, presumably due to oblique sectioning of rod-shaped nuclei (cc₃). The chief cells give off processes which occasionally are longitudinally cut (cc₂ - arrow), but most often transversely (asterisks). The chief-cell cytoplasm shows varying electron transparency, compare cc₁ with cc₄. The cells are lying between vascular lumina (ve), and nerve fibres (nf) course between the cells.

Magnification: $\times$ 4,800.

5.23

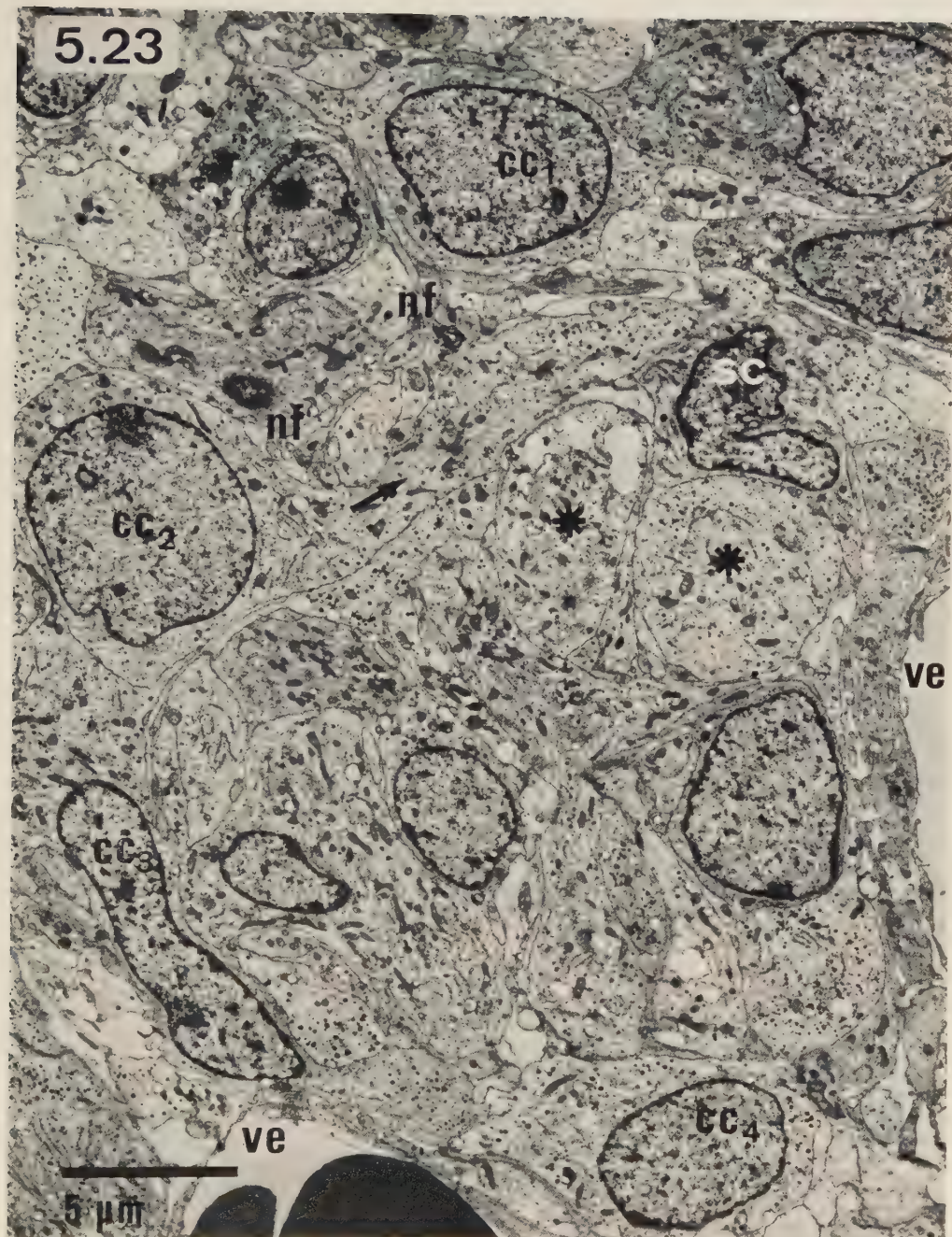


Fig. 5.24.

Vessel. Right subclavian glomus cr 62.

The wall around the vessel (ve) is formed by endothelium (en) and a perivascular cell (pc) enveloping by its extensions (arrow) a great part of the vessel, thereby forming a barrier between the vascular lumen and the glomus cells (cc, sc).

Magnification: $\times 6,800$.

Fig. 5.25.

Endothelial fenestrae. Right subclavian glomus cr 62.

Further magnification of the framed area in Fig. 5.24 showing that the endothelium contains pores (ep). Between the chief-cell process (cc), which is only partially invested by a supporting cell (cf. Fig. 5.24), and the vessel there is a wide amorphous interstice (is), part of a pericyte (pc), and collagen fibres (cf).

Magnification: $\times 30,000$.

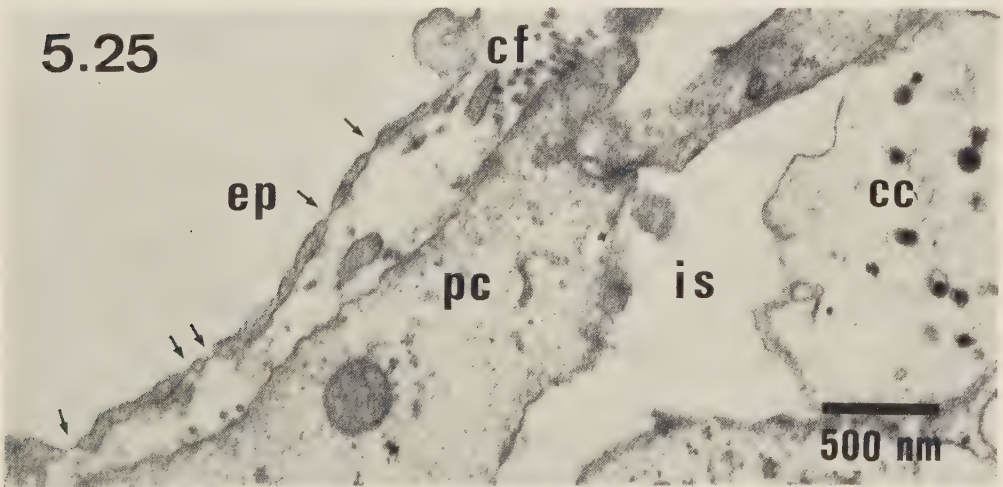
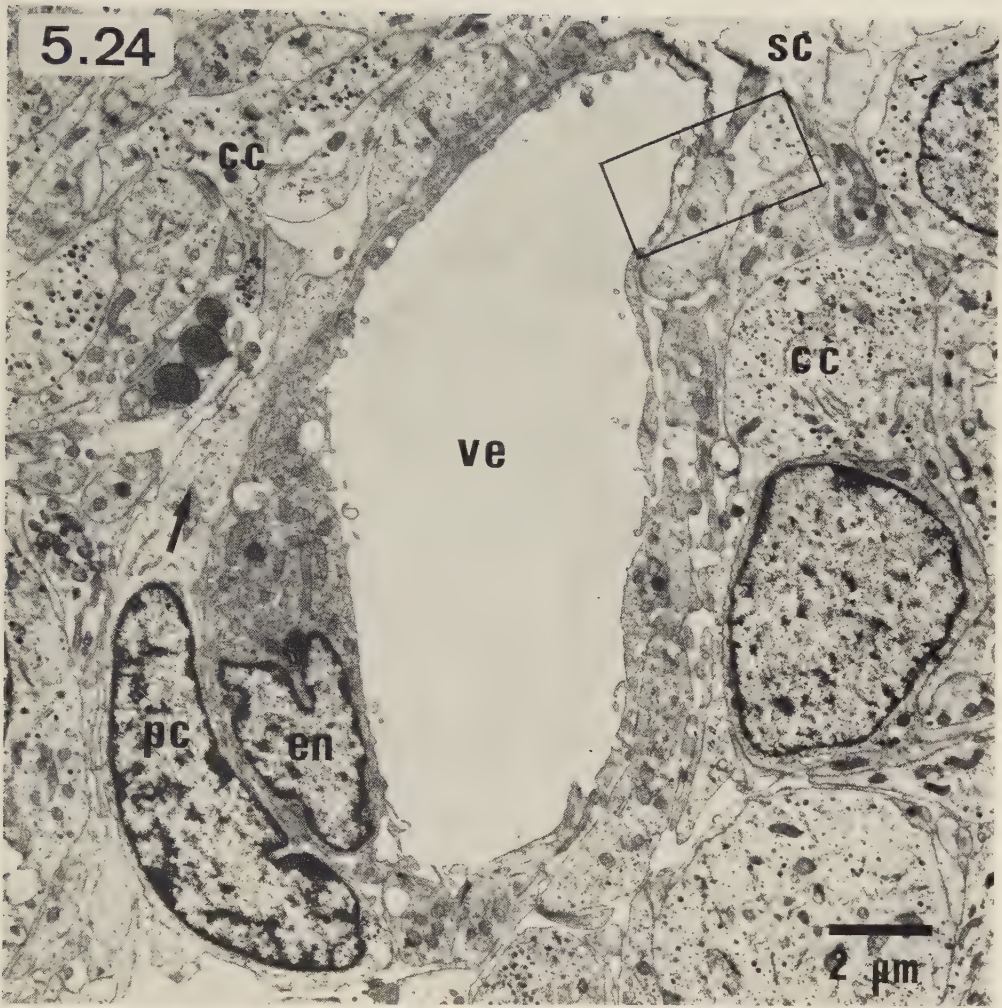


Fig. 5.26.

Relationship between chief and supporting cells. Right subclavian glomus cr 62.

Chief cell (cc_1) almost completely invested by very thin cytoplasmic processes (arrows) assumed to take their origin from a supporting cell. Nucleolus (nl), electron-dense body (db), chief cell with pale cytoplasm (cc_2), and specific granules (sg).

Magnification: $\times 14,200$.

Fig. 5.27.

Relationship between chief and supporting cells. Right subclavian glomus cr 62.

Magnification of a supporting cell (sc) from Fig. 5.23. The chromatin structure of the supporting cell is somewhat denser than in the chief cell shown above and exhibits a much more irregular shape. The cell is clinging around a chief cell (cc). Between the two cells nerve fibres (nf) are coursing.

Magnification: $\times 15,200$.

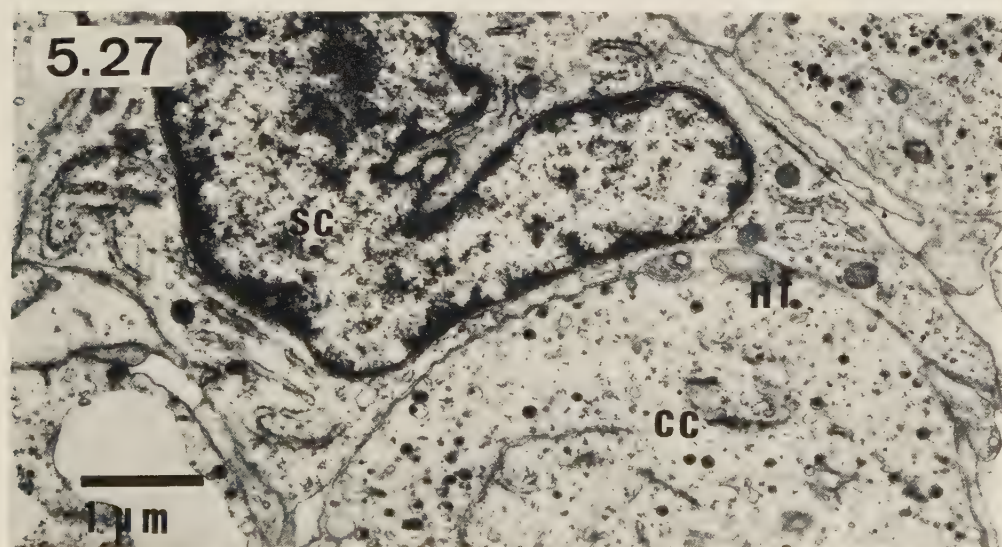
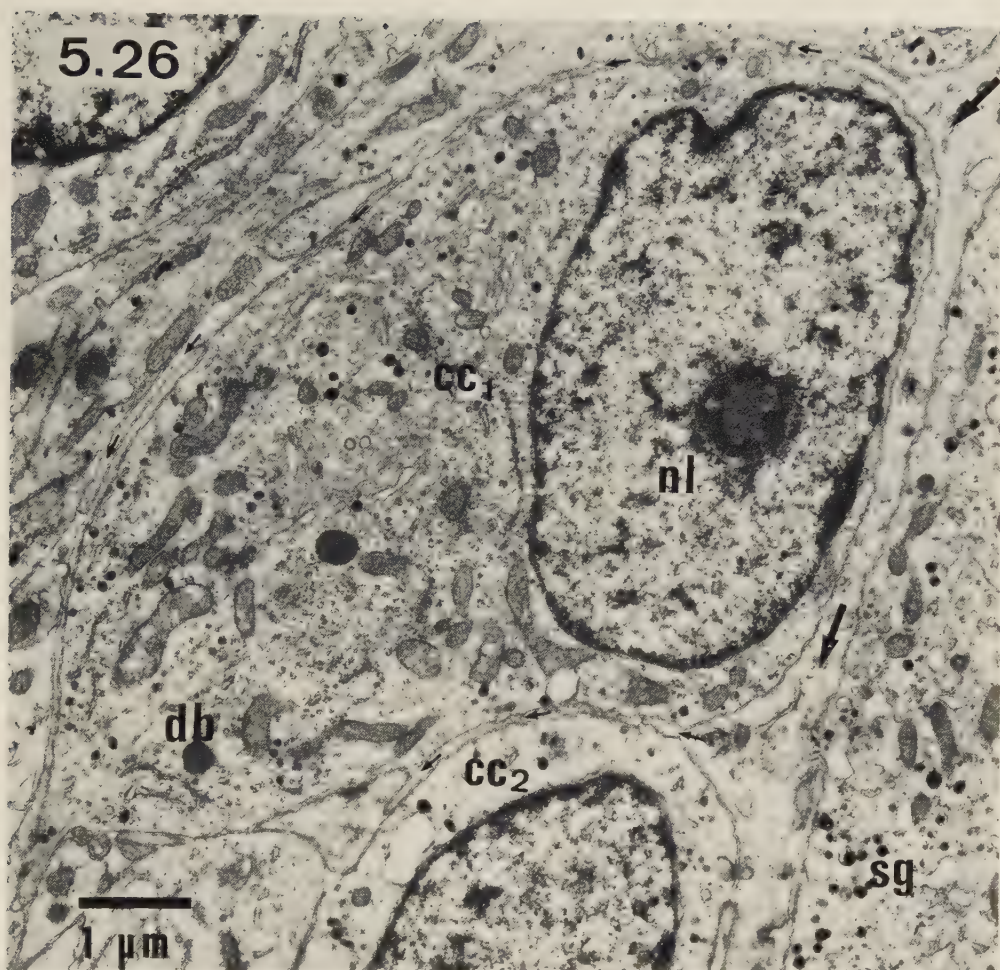


Fig. 5.28.

Organelles in chief cell. Right subclavian glomus cr 62.

Plasma membranes of two chief cells showing a slightly undulating and parallel course (arrows). In the cytoplasm of the cells granular endoplasmic reticulum (ger), vacuoles (va), Golgi zones (g), mitochondria (m), osmiophilic granules (sg), and a cilium-like structure (ci).

Magnification: $\times 18,800$.

Fig. 5.29.

Golgi zone in chief cell. Right subclavian glomus cr 62.

The Golgi complex (g) contains flat cisterns (1), vacuoles with pale contents (2), and vesicles with somewhat darker contents (3). In a cistern (at g) there is an accumulation of electron-dense material. One cistern, which judging by its ribosome content must belong to the endoplasmic reticulum, is possibly connected, on the agranular side, with vesicles (vs) of the same appearance as those contained in the Golgi zone (3). Chromatin (ch), nuclear pore (np), multi-vesicular body (vcb), specific granules (sg).

Magnification: $\times 71,300$.

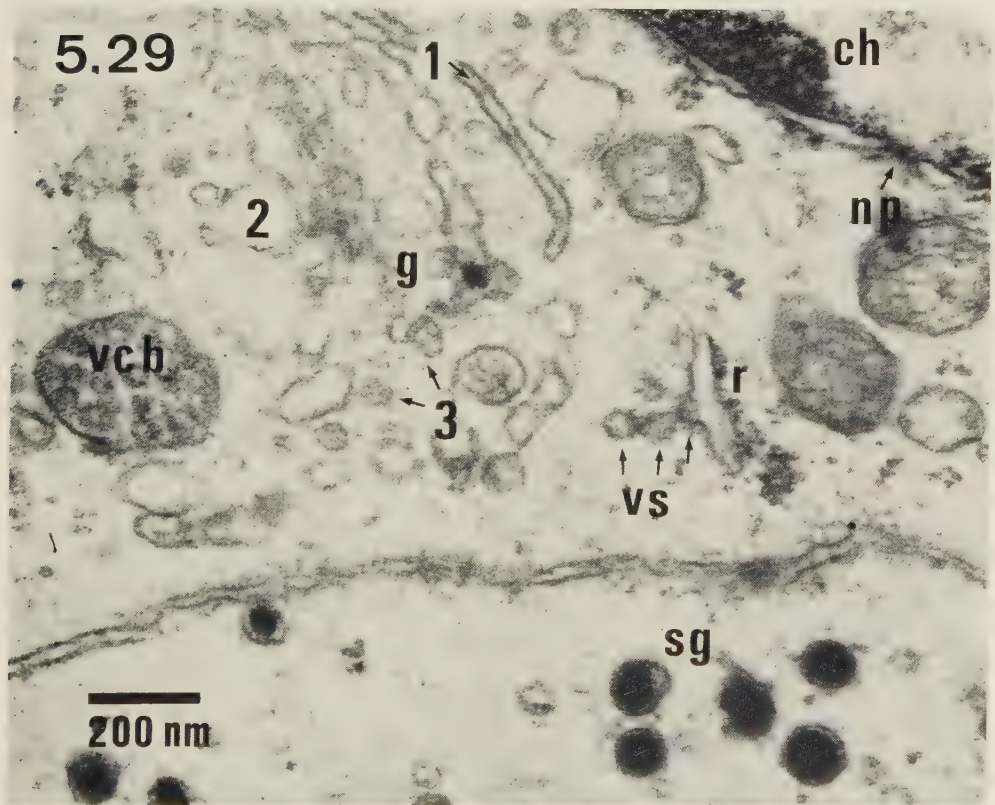
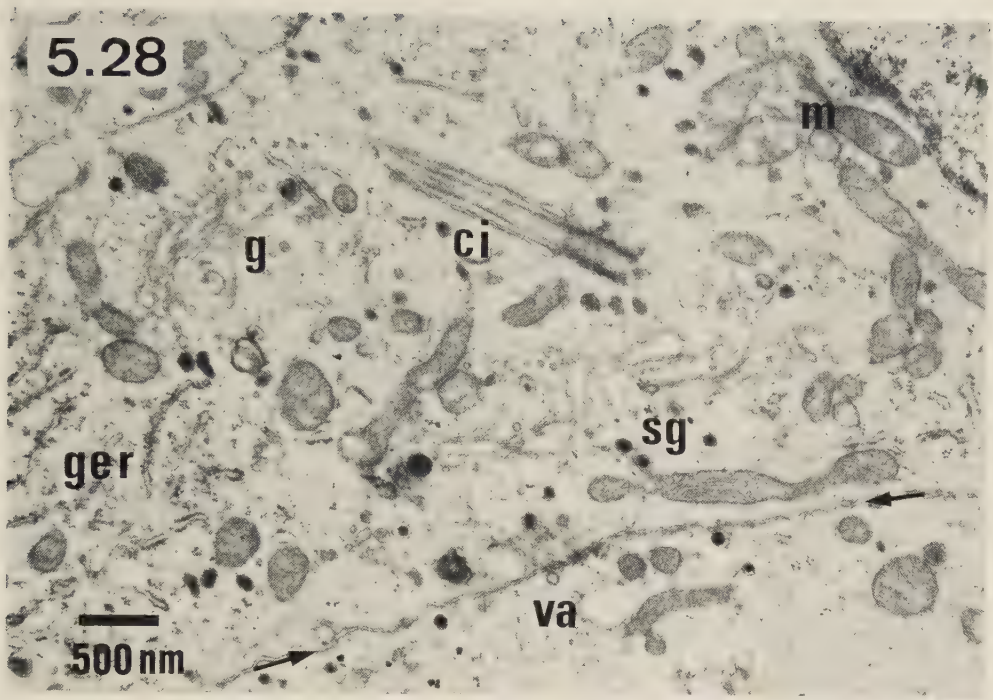


Fig. 5.30.

Nerve fibres. Right subclavian glomus cr 62.

Between a supporting cell (sc) and a chief cell with specific granule (sg) there are nerve fibres (nf). Their tubules (nt) are indistinguishable from those in the chief cell (mt).

Magnification: $\times 82,700$.

Fig. 5.31.

Detail of chief cells. Right subclavian glomus cr 62.

Mitochondrial granule (m), desmosome (d-d), agranular cisterns (aer), poly-ribosomes (r_1), solitary ribosomes (r_2), membrane-bound ribosomes (r_3), specific granules (sg).

Magnification: $\times 57,000$.

Fig. 5.32.

Detail of chief cell. Right subclavian glomus cr 62.

Specific granule (sg) with vesicle (3), pale corona (2), and structureless osmiophilic core (1). Longitudinally sectioned microtubule (mt).

Magnification: $\times 114,000$.

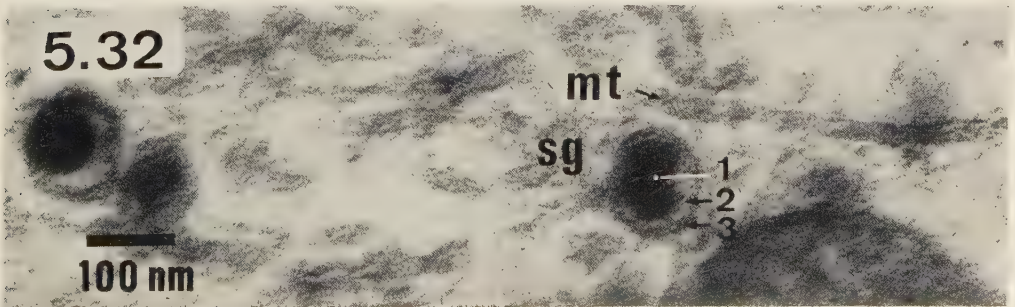
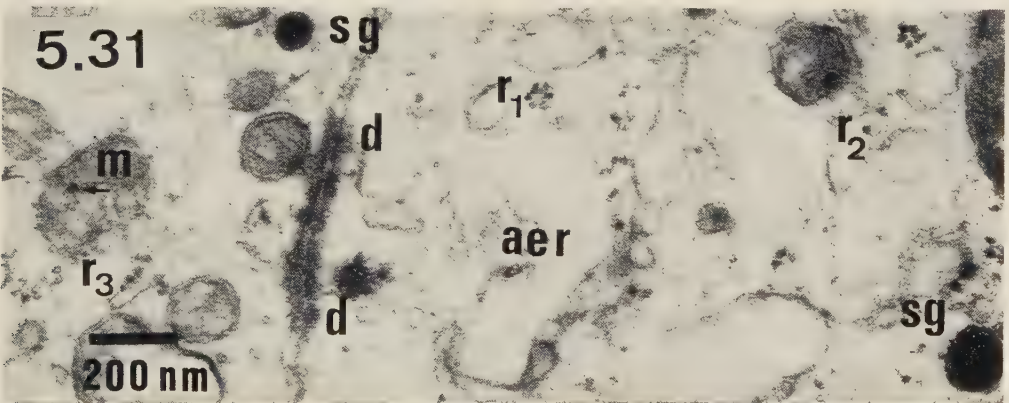
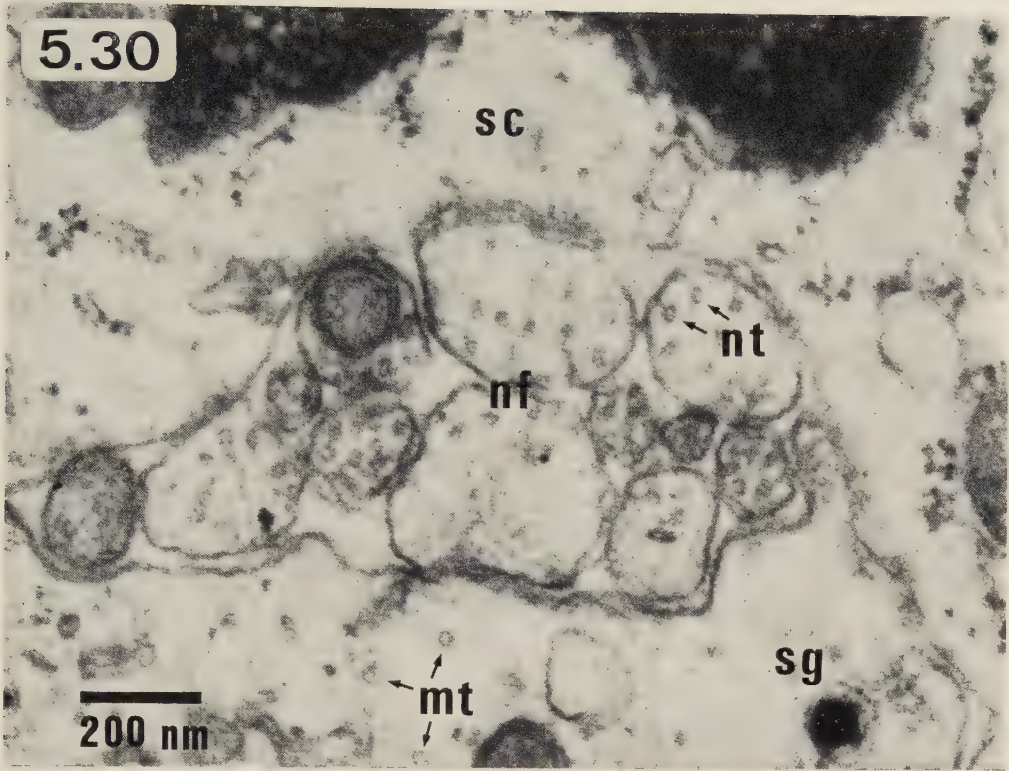


Fig. 6.1.

Example of specimen stepwise sectioned in order to locate glomera belonging to the tympanojugular glomus. Foetus cr 55.

Preparations in which it was possible to trace the intratympanic course of the tympanic branch of the glossopharyngeal nerve contained more tissue antero-medially than in the example shown. The preparations were embedded in Beem capsules, the posterior surface of the petrous portion of the temporal bone lying against the flat end of the capsules, making up the future face of the pyramid from which survey sections and ultra-thin sections were cut. The photograph was taken by transillumination of the dehydrated and resin-imbibed preparation from the right jugular foramen.

Magnification: ca. $\times 10$.

1. Jugular foramen, larger lateral part.
2. Spinal roots of accessory nerve.
3. Superior ganglion of vagus nerve.
4. Inferior ganglion of glossopharyngeal nerve.
5. Superior ganglion of glossopharyngeal nerve.
6. Vestibular part of the otic vesicle with the utricle and semicircular canals.

Fig. 6.2.

Light microscopic low power view. Tympanojugular glomus foetus cr 55.

Survey section cut parallel to the posterior surface of the petrous portion of the temporal bone through the jugular foramen of the preparation illustrated in Fig. 6.1. In relation to the auricular branch of the vagus nerve (4) cells suggestive of a glomus (cf. Fig. 6.3).

Magnification: $\times 40$.

1. Internal jugular vein, superior bulb.
2. Vagus nerve, area between superior and inferior ganglion.
3. Cranial part of the inferior ganglion of the glossopharyngeal nerve.
4. Auricular branch of the vagus nerve, main trunk.
5. Vagus-derived roots of the auricular branch of the vagus nerve.
6. Glossopharyngeal nerve-derived root of the auricular branch of the vagus nerve.
7. The cartilaginous primordium of the otic capsule.
8. Semicircular canal.

Fig. 6.3.

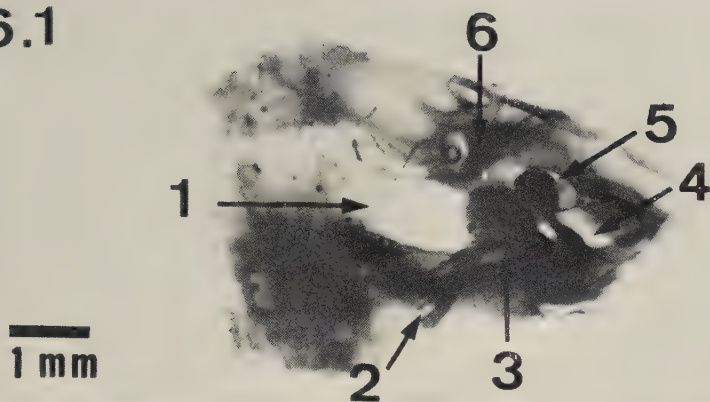
Light microscopic micrograph. Tympanojugular glomus foetus cr 55.

Higher magnification of the area marked 4 in Fig. 6.2 showing the auricular branch of the vagus nerve. The suspicious cells (2) which are almost embedded in the nerve are not in immediate contact with any vessels.

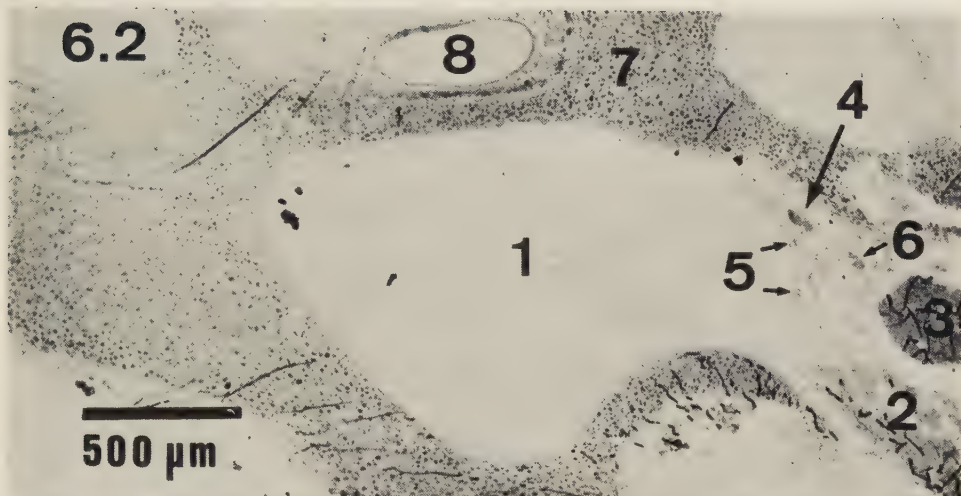
Magnification: $\times 640$.

1. Internal jugular vein.
2. Glomus cells.
3. Twigs of the auricular branch of the vagus nerve.

6.1



6.2



6.3

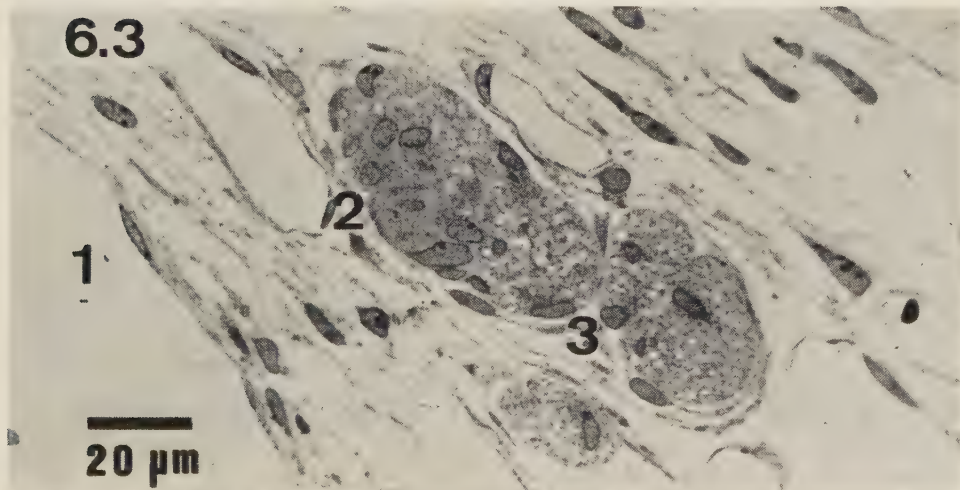


Fig. 6.4.

Light microscopic low power view. Tympanojugular glomus foetus cr 62a.

Survey section showing the situation of suspicious cells in relation to the tympanic branch of the glossopharyngeal nerve (6) shortly after its origin in the caudal part of the inferior ganglion of the glossopharyngeal nerve (5).

Magnification: $\times 40$.

1. Internal jugular vein, superior bulb.
2. Inferior ganglion of vagus nerve.
3. Inferior petrous sinus.
4. Superior cervical ganglion.
5. Caudal part of inferior ganglion of glossopharyngeal nerve.
6. Tympanic branch of the glossopharyngeal nerve with cellular condensation.
7. Basal turn of the primitive cochlea.
8. Mesenchyme in the future tympanic cavity.
9. Auricular branch of the vagus nerve.

Fig. 6.5.

Light microscopic micrograph. Tympanojugular glomus cr 62a.

Higher magnification of a section through the cells marked 6 in Fig. 6.4. The cells are situated in intimate relation to a thin-walled vessel (5). On the basis of the shape and situation of the cells, a tentative distinction may be made between chief cells (1) with pale, regularly shaped nuclei, and supporting cells (2) with irregular nuclei, adapting their shape to the neighbouring cells. Endothelial cells (3), possibly perivascular cells (4).

Magnification: $\times 640$.

1. Chief cells.
2. Supporting cells.
3. Endothelial cells.
4. ? Pericytes.
5. Vessel.
6. Tympanic branch of the glossopharyngeal nerve, cf. Fig. 6.4.

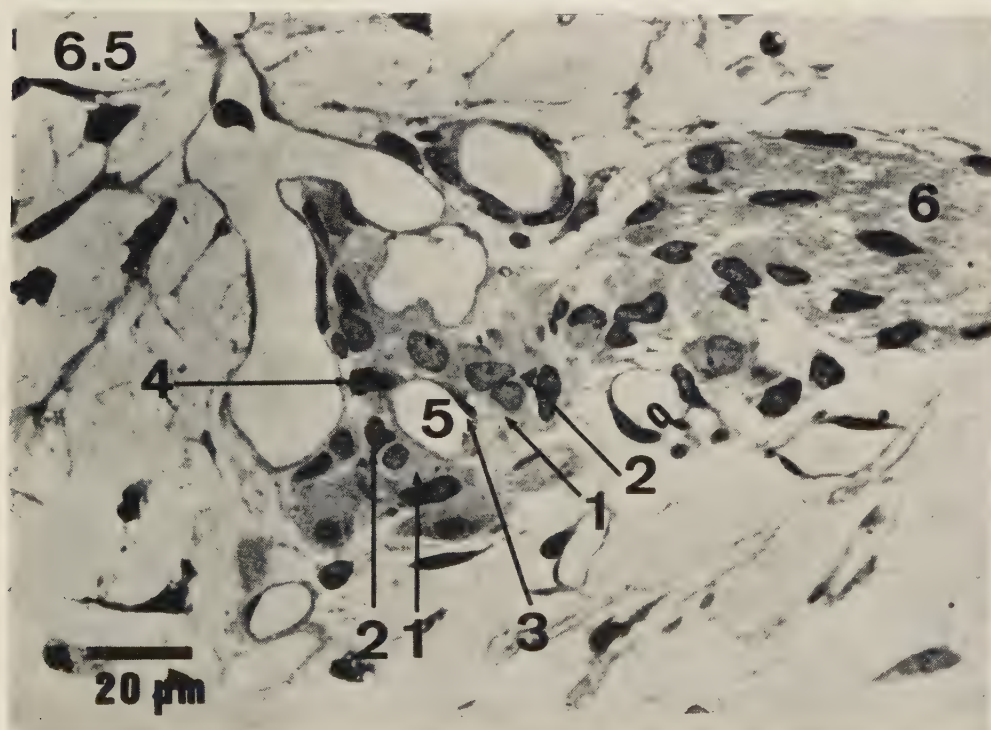
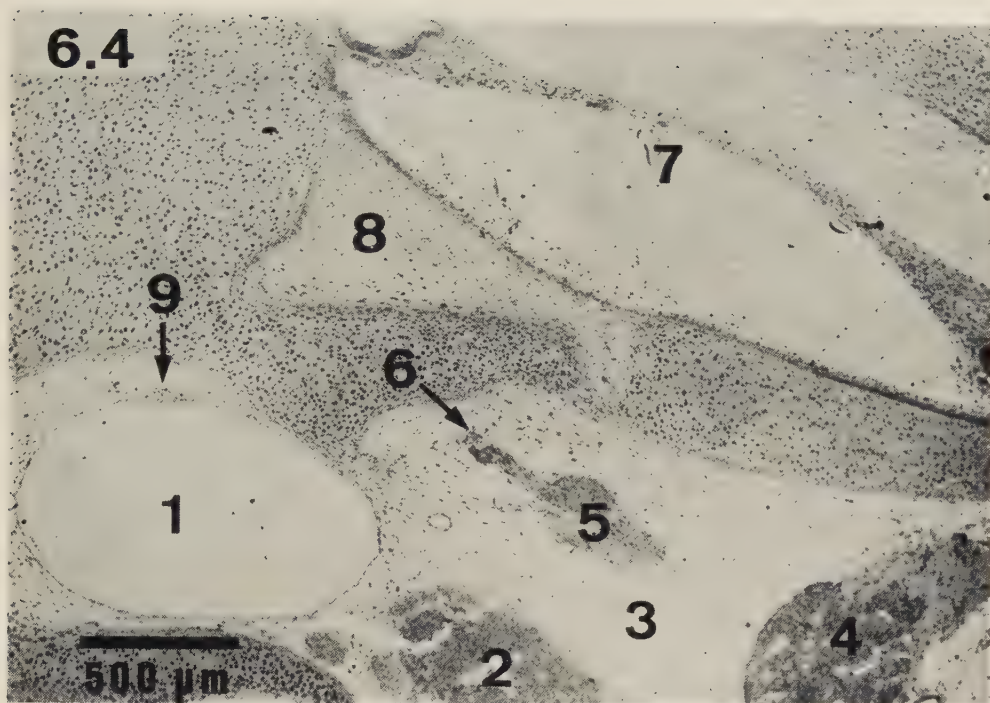


Fig. 6.6.

Light microscopic low power view. Tympanojugular glomus cr 62b.

Survey section showing the situation of glomus cells in relation to the tympanic branch of the glossopharyngeal nerve (2), immediately before it enters the tympanic canaliculus.

Magnification: $\times 40$.

1. Internal jugular vein, superior bulb.
2. Tympanic branch of the glossopharyngeal nerve.
3. Basal turn of the primitive cochlea.
4. Mesenchyme in the future tympanic cavity.
5. The cartilaginous primordium of the otic capsule.
6. Auricular branch of the vagus nerve.
7. Semicircular canal.
8. Anastomotic branch between auricular branch of the vagus nerve and the glossopharyngeal nerve.

Fig. 6.7.

Light microscopic micrograph. Tympanojugular glomus cr 62b.

Magnification of the area marked 2 on Fig. 6.6, showing a group of glomus cells (3) situated between the fibres of the tympanic branch of the glossopharyngeal nerve (1) and the floor of the tympanic cavity (5). The cell group is surrounded by thin-walled vessels whose endothelium, in parts of the vascular circumference, directly adjoins the cells (4).

Magnification: $\times 640$.

1. Tympanic branch of the glossopharyngeal nerve.
2. ? Primordium of inferior tympanic artery.
3. Glomus cells.
4. Contact with vessels.
5. Primordium of floor of tympanic cavity.

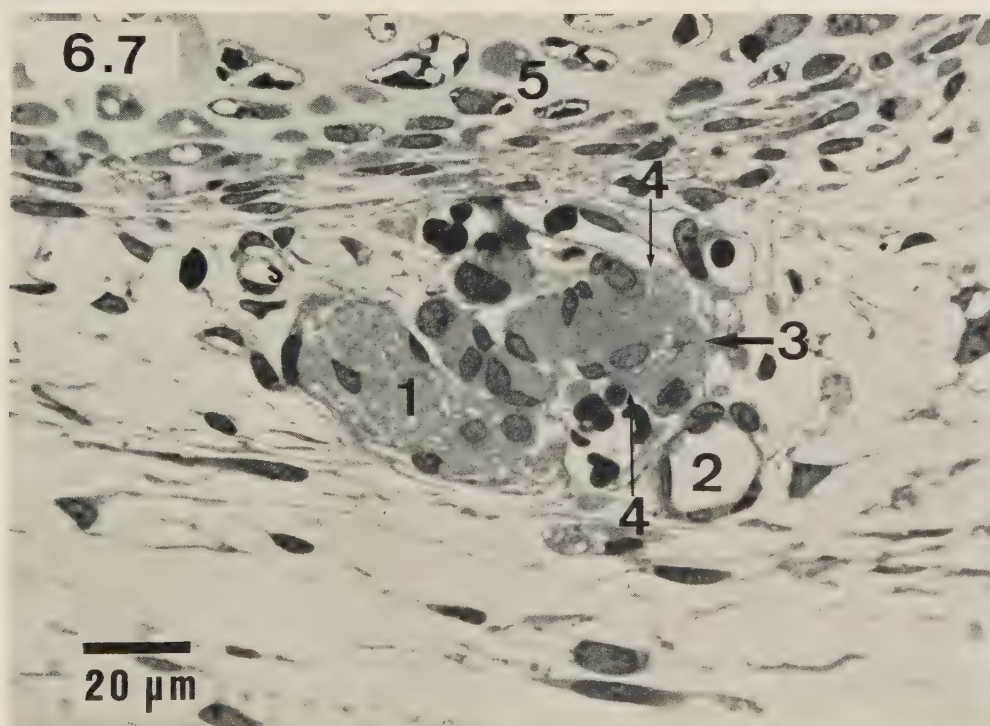
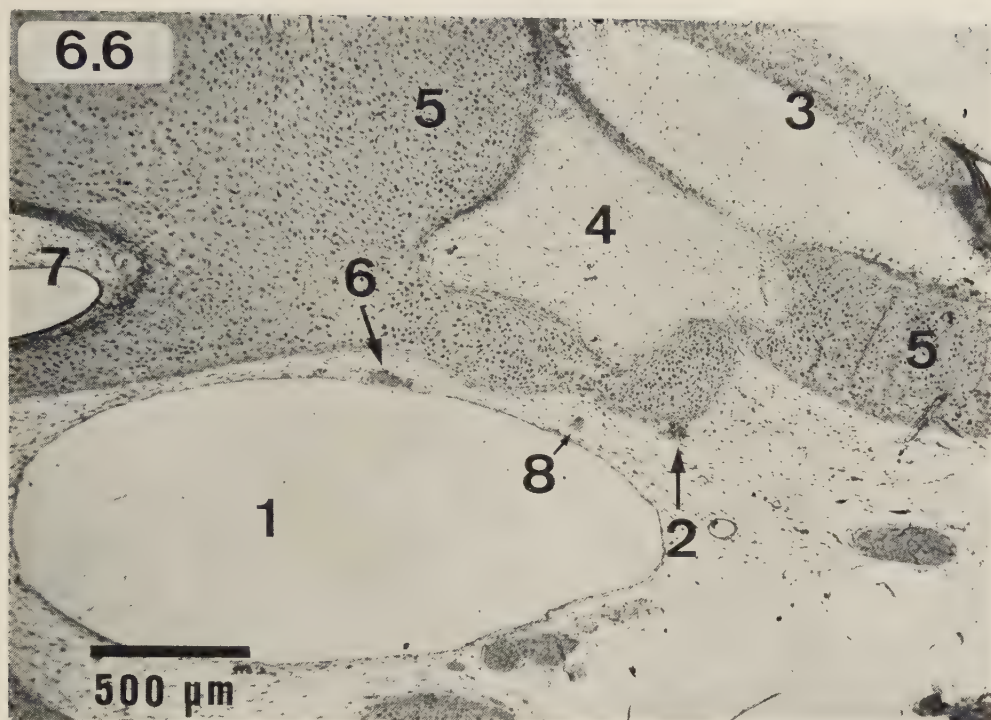


Fig. 6.8.

Light microscopic low power view. Tympanojugular glomus cr 62c.

Survey section showing the auricular branch of the vagus nerve (8), situated in the adventitia of the superior bulb of jugular vein (1). A glomus at the indicated site at the auricular branch of vagus nerve, cf. Fig. 6.9.

Magnification: $\times 40$.

1. Internal jugular vein, superior bulb.
2. Tympanic branch of the glossopharyngeal nerve.
3. Glossopharyngeal nerve sectioned caudally to the inferior ganglion.
4. Cartilaginous ear capsule.
5. Basal turn of the cochlea sectioned tangentially.
6. Primitive tympanic cavity filled with loose mesenchyme.
7. Tympanic canaliculus exhibiting the nature of a foramen.
8. Auricular branch of the vagus nerve.

Fig. 6.9.

Light microscopic micrograph. Tympanojugular glomus cr 62c.

High magnification of a section situated about 5 μ m more peripherally along the auricular branch of the vagus nerve than that in Fig. 6.8 with 8 marked areas. Interposed between the axon bundles in the auricular branch of the vagus nerve (4) and the endothelial layer in the internal jugular vein (3) two groups of glomus cells (1). One group is separated from the nerve by a thin-walled vessel (2).

Magnification: $\times 640$.

1. Glomus cells.
2. Vessel.
3. Endothelial cells in the wall of the internal jugular vein.
4. Auricular branch of the vagus nerve.

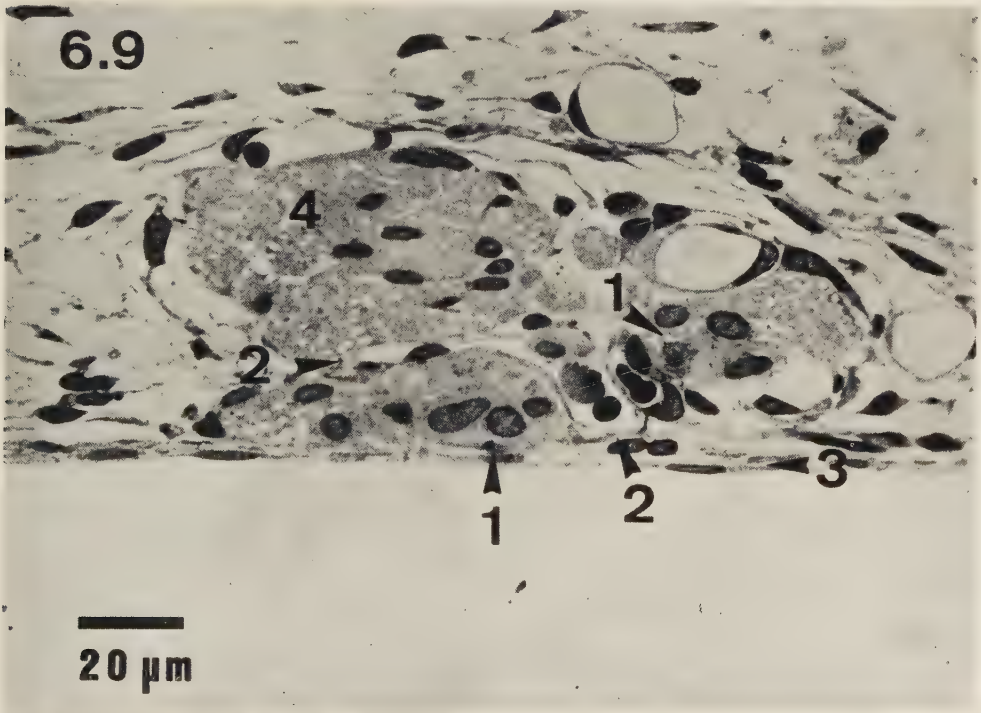
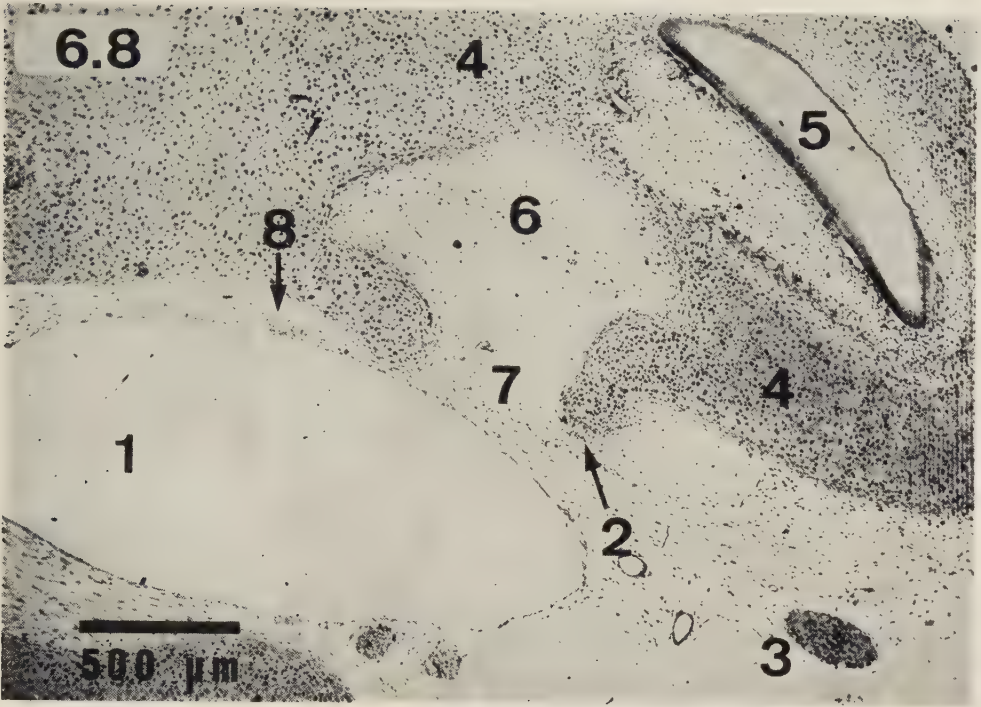


Fig. 6.10.

Light microscopic low power view. Tympanojugular glomus cr 62d.

Survey section showing the situation of a small glomus (12) embedded laterally in the superior bulb of the jugular vein (2). The glomus is not in immediate relation to the auricular branch of the vagus nerve which in this section is situated in the mastoid canaliculus (13).

Magnification: $\times 40$.

1. Mastoid process.
2. Internal jugular vein.
3. Accessory nerve.
4. Inferior ganglion of vagus nerve.
5. Inferior petrous sinus.
6. Glossopharyngeal nerve, area peripheral to the ganglia.
7. Superior cervical ganglion.
8. Internal carotid artery.
9. Basal turn of cochlea.
10. Tympanic branch of the glossopharyngeal nerve on the promontory.
11. Loose mesenchyme in the future tympanic cavity.
12. Glomus (cf. Fig. 6.11).
13. Auricular branch of the vagus nerve in the mastoid canaliculus.

Fig. 6.11.

Light microscopic micrograph. Tympanojugular glomus cr 62d.

Magnification of the area marked 12 in Fig. 6.10 containing a small, well-defined group of cells (1) apparently supplied by an independent vessel (2).

Magnification: $\times 640$.

1. Glomus.
2. ? Glomus vessel.
3. Internal jugular vein.

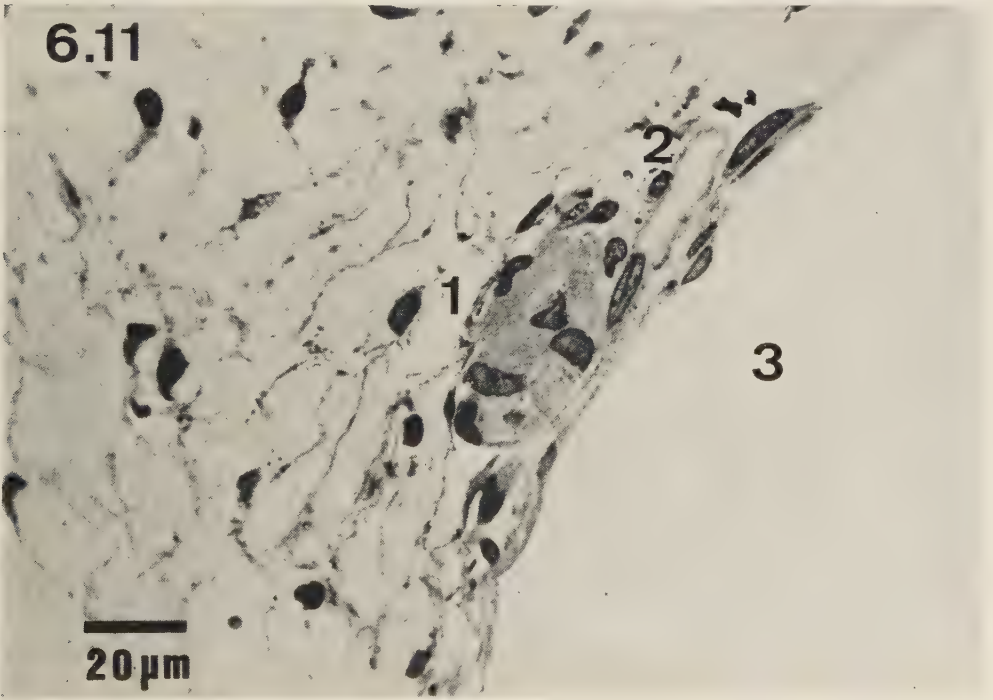
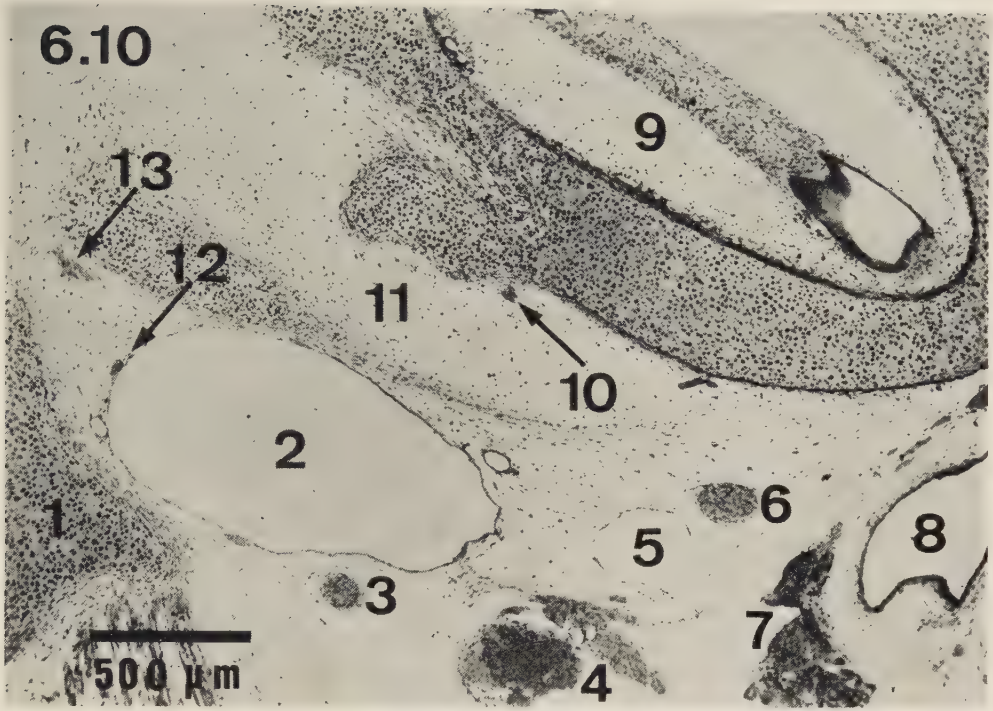


Fig. 6.12.

Light microscopic low power view. Tympanojugular glomus cr 62e.

Survey section showing the situation of a glomus (7) between the superior bulb of the jugular vein (2) and the floor (6) of the tympanic cavity. The auricular branch of the vagus nerve has passed the superior bulb in the same sagittal plane, but farther cranio-posteriorly. In this section it is situated laterally in the mastoid canaliculus (8).

Magnification: $\times 40$.

1. Mastoid process.
2. Internal jugular vein, superior bulb.
3. Glossopharyngeal nerve.
4. Basal turn of cochlea.
5. Tympanic branch of the glossopharyngeal nerve.
6. Primordium of floor of tympanic cavity.
7. Glomus, cf. Fig. 6.13.
8. Auricular branch of the vagus nerve laterally in the mastoid canaliculus.
9. Descending facial canal. The nerve is not included at the illustrated level.

Fig. 6.13.

Light microscopic micrograph. Tympanojugular glomus cr 62e.

Magnification of the area marked 7 in Fig. 6.12. The glomus (1) is very vascular (2) considering its size. No nerve fibres are demonstrable by the technique used. The majority of cells are assumed to be chief cells (4), a few supporting cells (3).

Magnification: $\times 640$.

1. Glomus.
2. Vessel.
3. Supporting cell.
4. Chief cell.
5. Internal jugular vein.

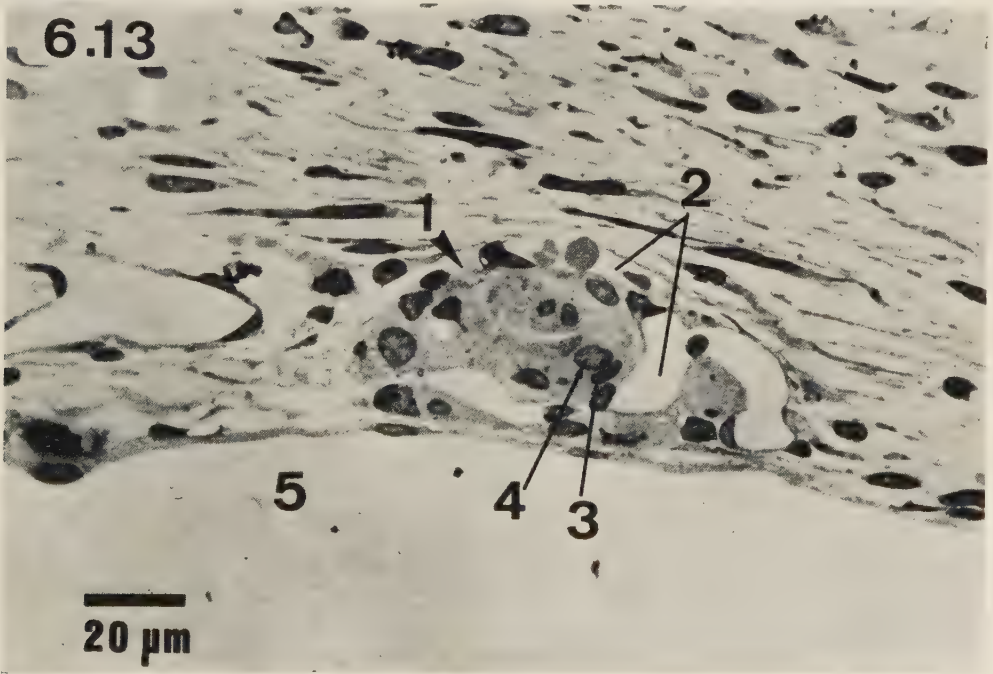
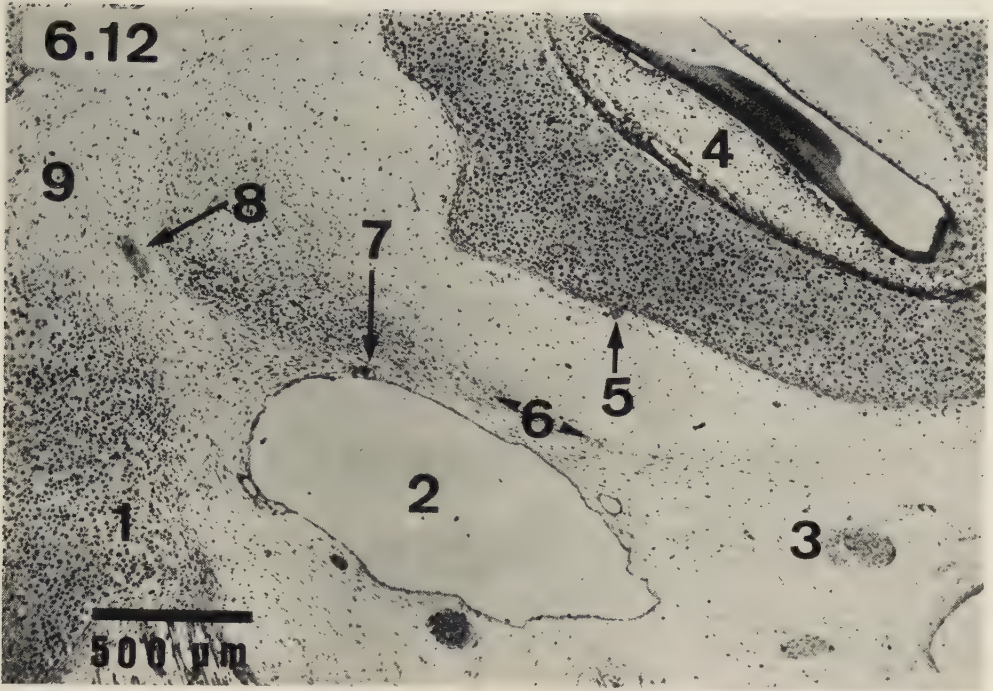


Fig. 6.14.

Light microscopic low power view. Tympanojugular glomus cr 62f.

The glomus (4) is situated periadventitially in the superior bulb of the internal jugular vein (1), approximately in that area of the bulb where the auricular branch of the vagus nerve – after having crossed the bulb in a periadventitial position (cf. e. g. Fig. 6.4) – leaves the venous wall in the direction to the mastoid canaliculus. The cartilaginous primordium of the bony cochlea on a level with the basal turn has been sectioned tangentially, so that the future promontory (2) is like an island in the mesenchyme which later is displaced by the expanding tympanic vesicle. The tympanic branch of the glossopharyngeal nerve (3) visible on both sides of the promontory.

Magnification: $\times 40$.

1. Superior bulb of the jugular vein.
2. Promontory.
3. Tympanic branch of the glossopharyngeal nerve.
4. Glomus, cf. Fig. 6.15.
5. Auricular branch of the vagus nerve.

Fig. 6.15.

Light microscopic micrograph. Tympanojugular glomus cr 62f.

Magnification of the area marked 4 in Fig. 6.14. The group of cells (1) is surrounded by small vessels whose endothelium in some areas (arrows) directly adjoins the glomus cells.

Magnification: $\times 640$.

1. Glomus cells.
2. Superior bulb of the jugular vein.

Arrows: Areas of contact.

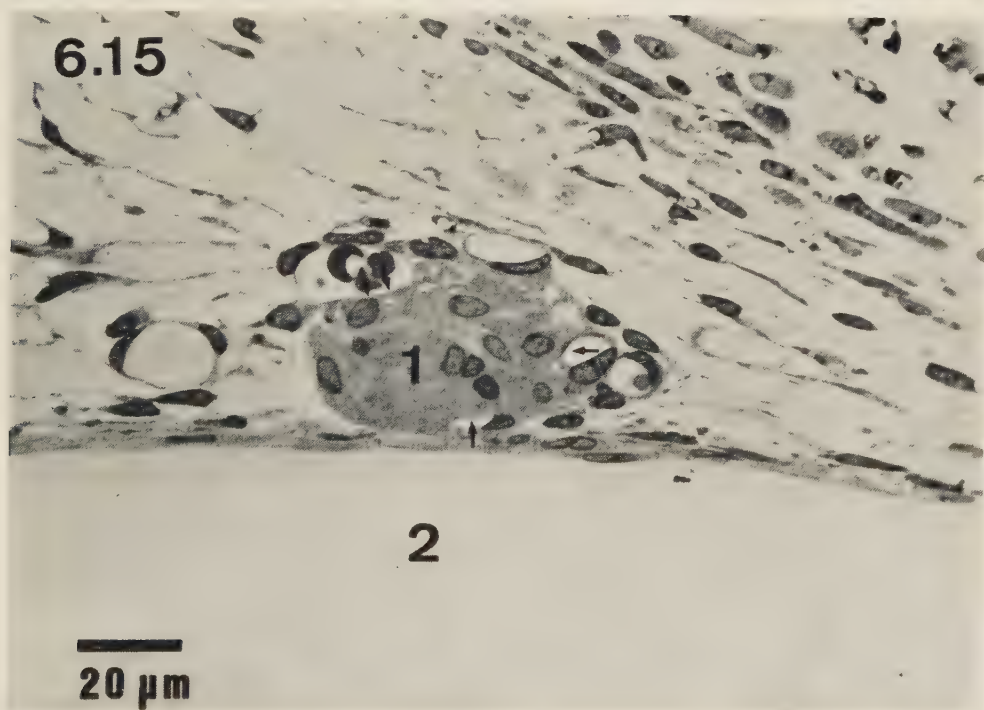
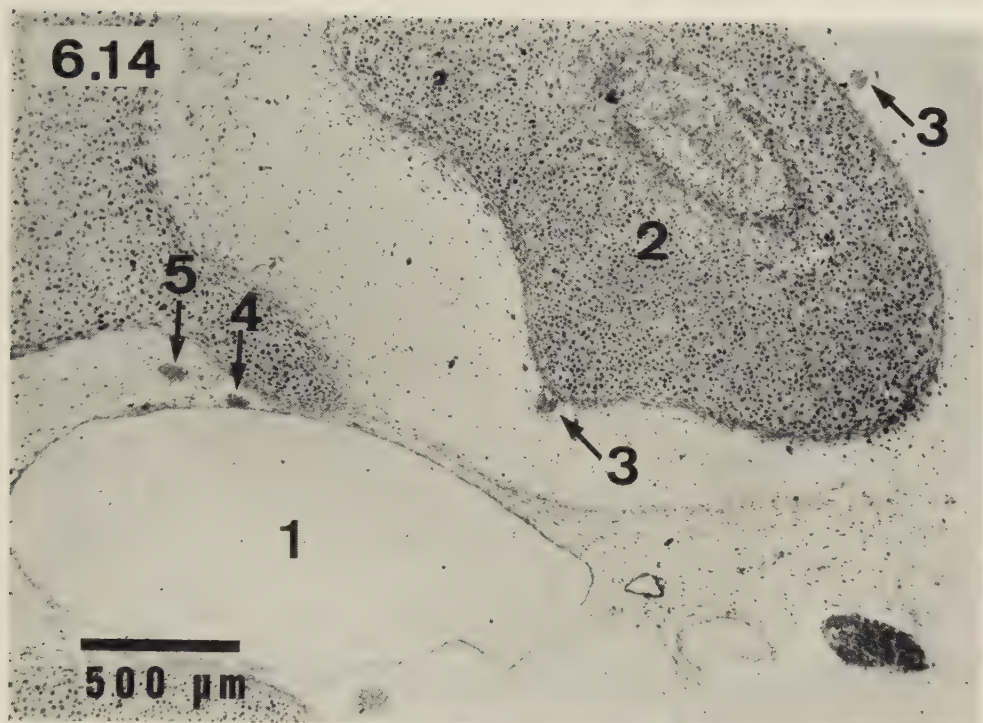


Fig. 6.16.

Light microscopic low power view. Tympanojugular glomus cr 59.

Survey section showing a glomus (5) situated in relation to the tympanic branch of the glossopharyngeal nerve on the course of the nerve on the medial wall of the tympanic cavity.

Magnification: $\times 40$.

1. Superior bulb of the jugular vein.
2. Area medial to the jugular vein has been traumatized, the vessel wall being torn off. The auricular branch of the vagus nerve could be traced to the traumatized area.
3. Primitive tympanic cavity.
4. Peritympanic connective tissue.
5. Tympanic branch of the glossopharyngeal nerve with glomus (cf. Fig. 6.17).
6. Promontory (cf. Fig. 6.14).
7. Tympanic branch of the glossopharyngeal nerve.

Fig. 6.17.

Light microscopic micrograph. Tympanojugular glomus cr 59.

Magnification of the area marked 5 in Fig. 6.16.

Magnification: $\times 640$.

1. Glomus cells.
2. Tympanic branch of the glossopharyngeal nerve.
3. Inferior tympanic artery.
4. Thin-walled vessel whose one side adjoins the glomus cells.
5. Cartilaginous primordium of the otic capsule on a level with the basal turn of the cochlea.
6. The perichondral connective tissue forms, together with the cartilage, a tunnel housing the nerve, vessels, and glomus.

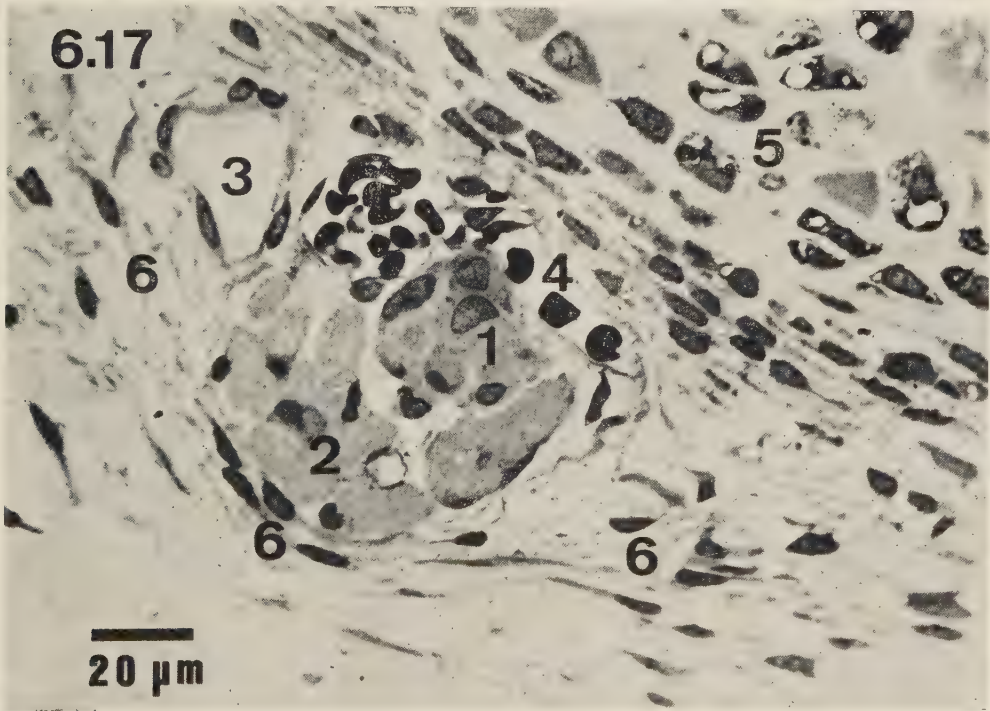
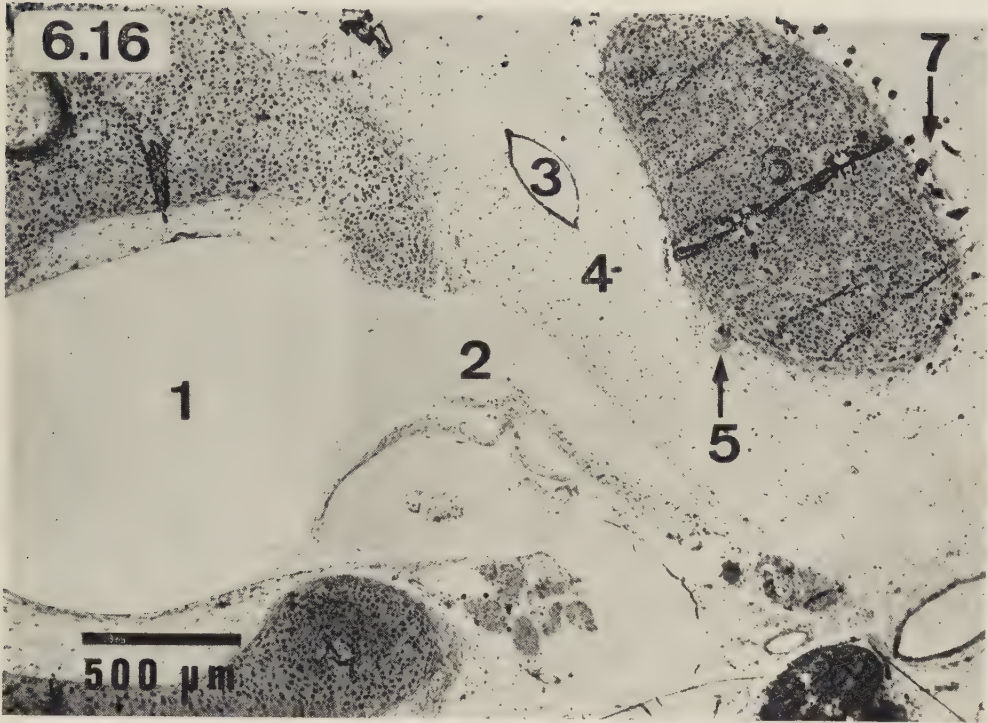


Fig. 6.18.

Electron microscopic low power view. Tympanojugular glomus cr 62c.

As was apparent from the light microscopic findings (cf. Fig. 6.9) the glomus is situated between the wall of the internal jugular vein (lu) and the auricular branch of the vagus nerve whose axon bundles are embraced by Schwann cells (sw). A vessel (ve) wedged in between the venous wall and the glomus cells. Among the latter chief cells (cc) predominate. At this magnification their osmophilic granules can just be discerned as dark dots. The chief cells show great variation in electron transparency (cf. e. g. cc₁ and cc₂). One of the cells sectioned through the nucleus is a supporting cell (sc). This cell, int. al., gives off long processes interspersed between the chief cells (arrows). In small areas the chief cells may be without mutual contact or supporting-cell cover, so that they communicate direct with the interstitial connective-tissue space (is). Nerve fibres (nf) course between the cells.

Magnification: $\times 3,800$.

6.18

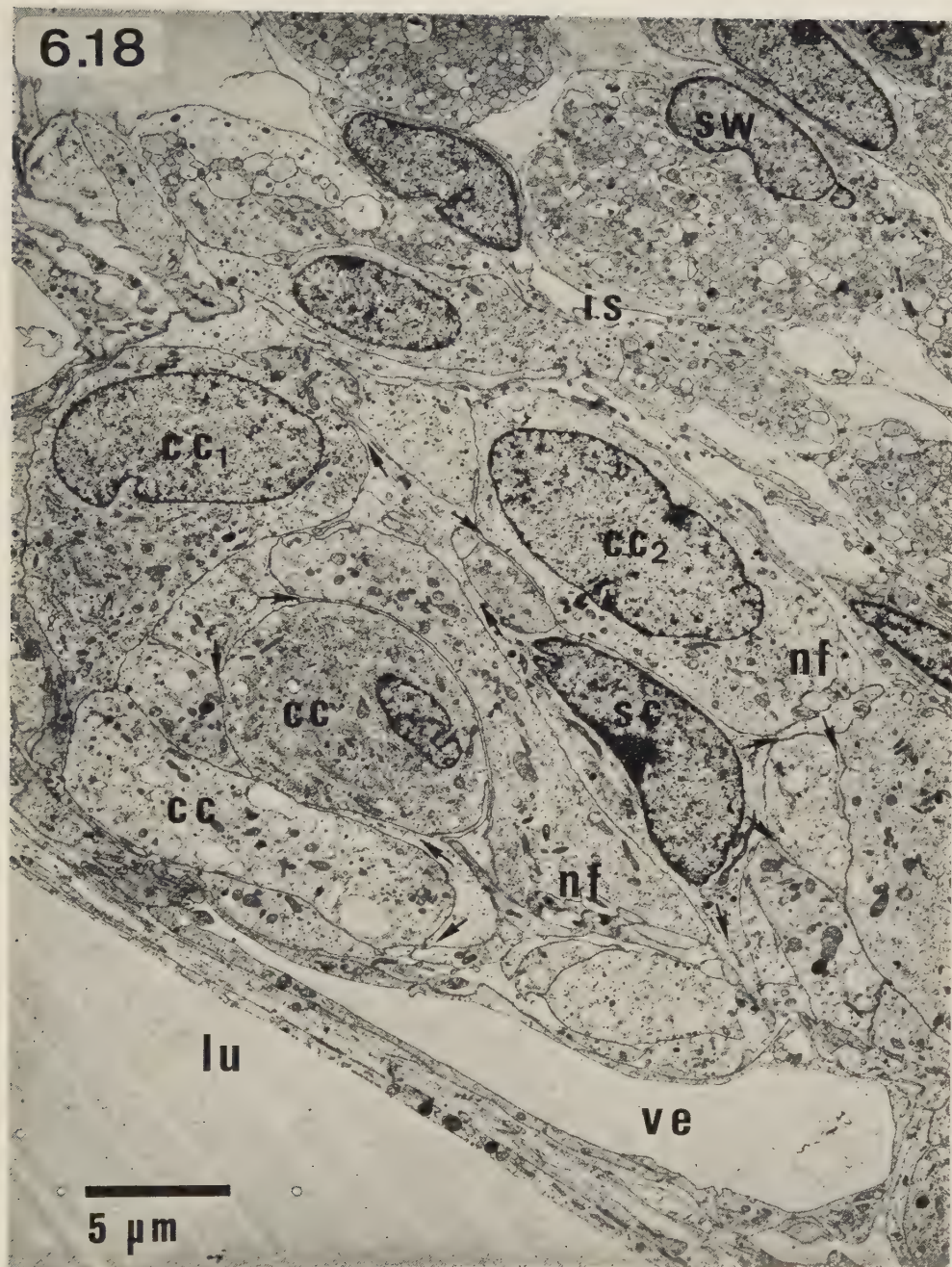


Fig. 6.19.

Electron microscopic low power view. Tympanojugular glomus cr 55.

Chief cell group (cc) invested by thin cytoplasmic extensions (arrows) separating the chief cells from axons (nf) belonging to the auricular branch of the vagus nerve (cf. Fig. 6.3) and from the surrounding connective tissue (ct). A few processes issue from a cell (sw) which also acts as supporting cell to the axons in the auricular branch of the vagus nerve. The supporting-cell processes also intrude partially between the chief cells. It will be noted that the chief cells also give off processes which in this section have been cut both longitudinally (pcc_1) and transversely (pcc_2) and that the number of osmiophilic granules per cell part is extremely varied.

Magnification: $\times 7,100$.

6.19

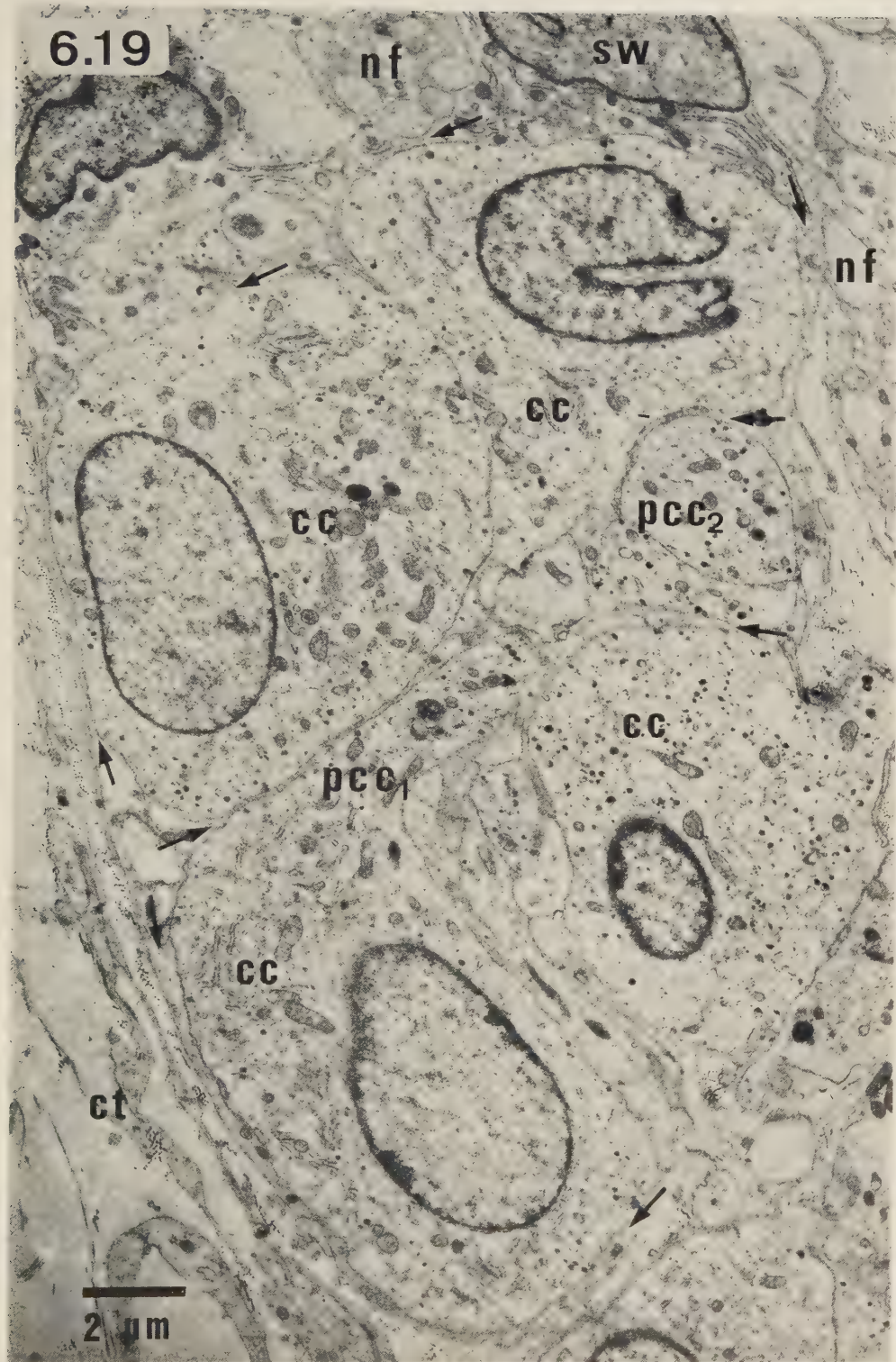


Fig. 6.20.

Electron microscopic low power view. Tympanojugular glomus cr 59.

Of the three cells sectioned through the nucleus two may be identified as chief cells (cc) with regular, relatively pale nuclei and one as a supporting cell (sc) with an irregularly shaped nucleus of a dense chromatin structure. The area between the chief cells is of a highly intricate architecture, being composed of chief cell parts (pcc), nerve fibres (nf), and thin processes (arrows).

Magnification: $\times 5,100$.

6.20

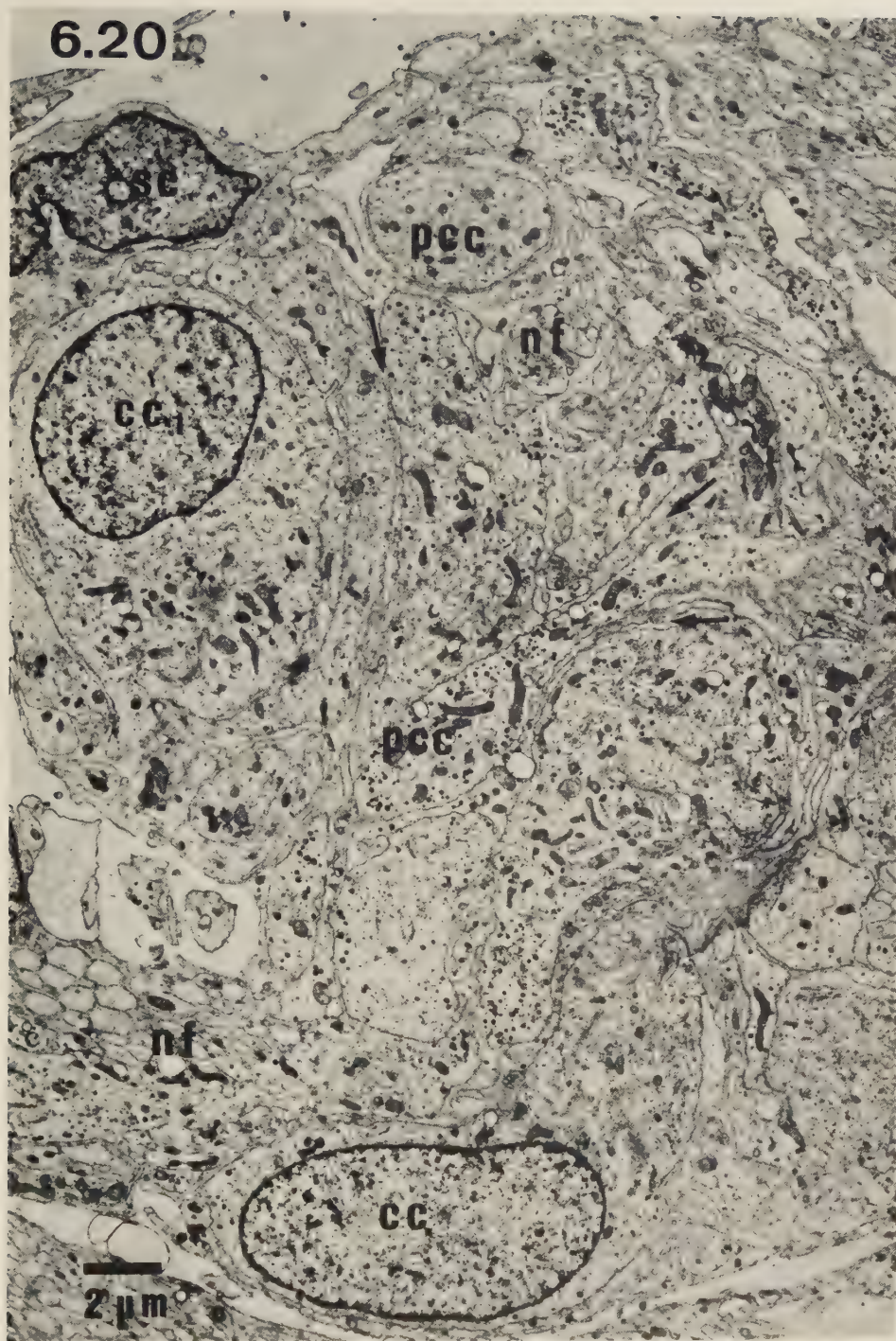


Fig. 6.21.

Vascular relations. Tympanojugular glomus cr 62e.

Glomus situated close to the internal jugular vein (cf. Fig. 6.13), whose lumen (lu) is visible in the picture. In the glomus two vascular lumina. The smaller one (ve₁) is entirely encapsulated by pericyte processes (pc₁). The endothelium of the other vessel (ve₂) adjoins similar pale cytoplasmic processes (pc₂, thick arrow) with chief cell parts (pcc₂, pcc₃) and non-identifiable cell processes (asterisks). A perivascular cell (pc₃) gives off a long process coursing concentrically with the endothelium (thick arrow). From this process arise secondary processes (thin arrows) partially investing chief cell parts (pcc₃, cc). The endothelial area marked ep is given in higher magnification in Fig. 6.22.

Magnification: $\times 5,300$.

Fig. 6.22.

Endothelial fenestration. Tympanojugular glomus cr 62e.

Higher magnification of the area marked ep in Fig. 6.21, showing parts of a chief cell (cc), pericyte (pc), vascular lumen (ve₂) and endothelium (en) with pores (ep). No basal lamina.

Magnification: $\times 73,500$.

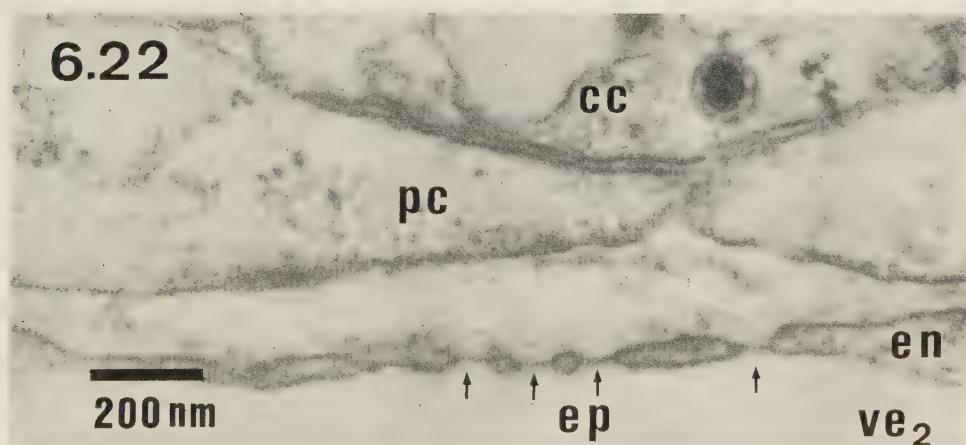
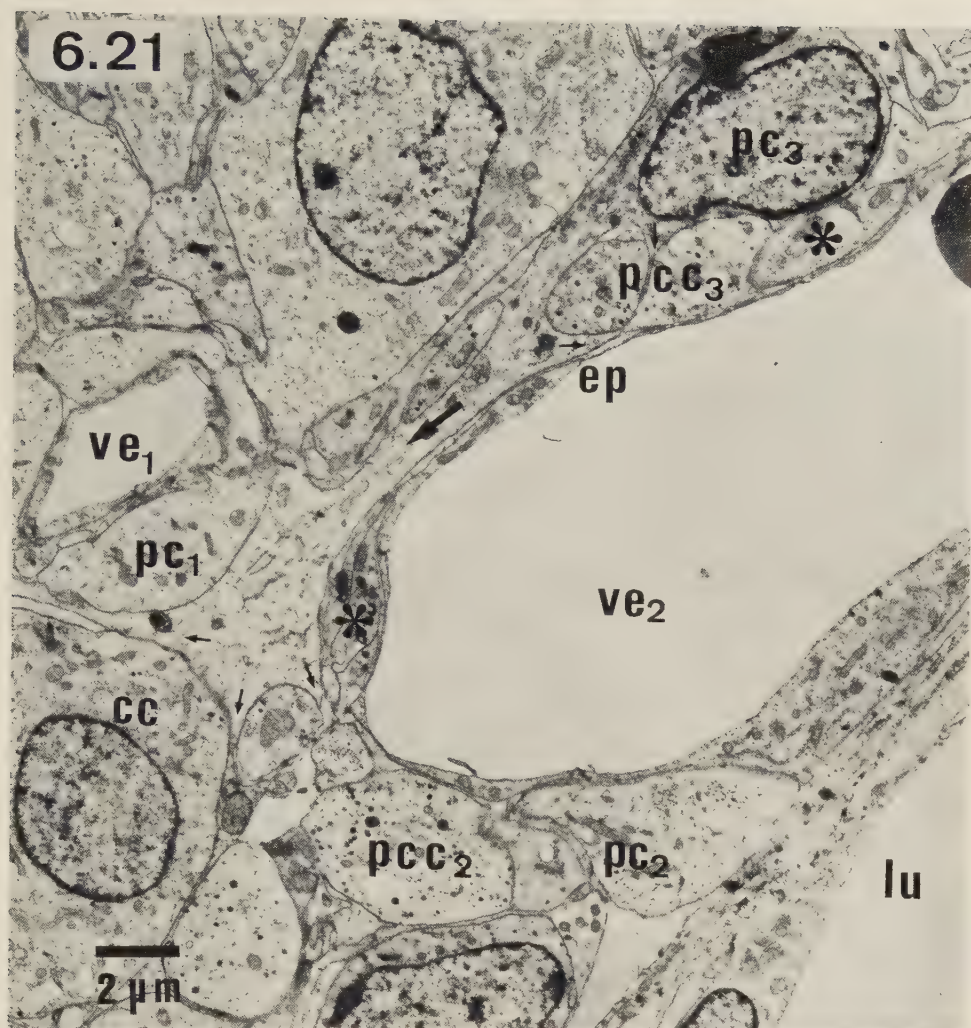


Fig. 6.23.

Relation between vessels and glomus cells. Tympanojugular glomus cr 62f.

At the top a vascular lumen (ve) invested by an endothelial cell (en) and a pericyte (pc). At the bottom a chief cell (cc) enveloped by a supporting-cell process (sc). In the middle on the left fibroblastic processes (fb), which may be recognized by the strikingly wide granular cisterns with relatively dark content, and on the right chief-cell processes (pcc) and nerve fibres (nf). The framed area is given in higher magnification in Fig. 6.24.

Magnification: $\times 8,000$.

Fig. 6.24.

Endothelial pores. Tympanojugular glomus cr 62f.

Magnification of the framed area of Fig. 6.23, showing that in the endothelium (en) there are pores (arrows) whose diaphragm is distinctly illustrated at least in the right and left pore. Between the endothelium and the pericytic process (pc) a delicately fibrillar or flocculent material (is_1) which, however, is so diffuse that it cannot be directly interpreted as a basal lamina. Corresponding material around the chief cell (pcc) in the short area where its plasma membrane does not directly adjoin the plasma membranes of other cells (is_2). Unidentified cell process (asterisk).

Magnification: $\times 59,900$.

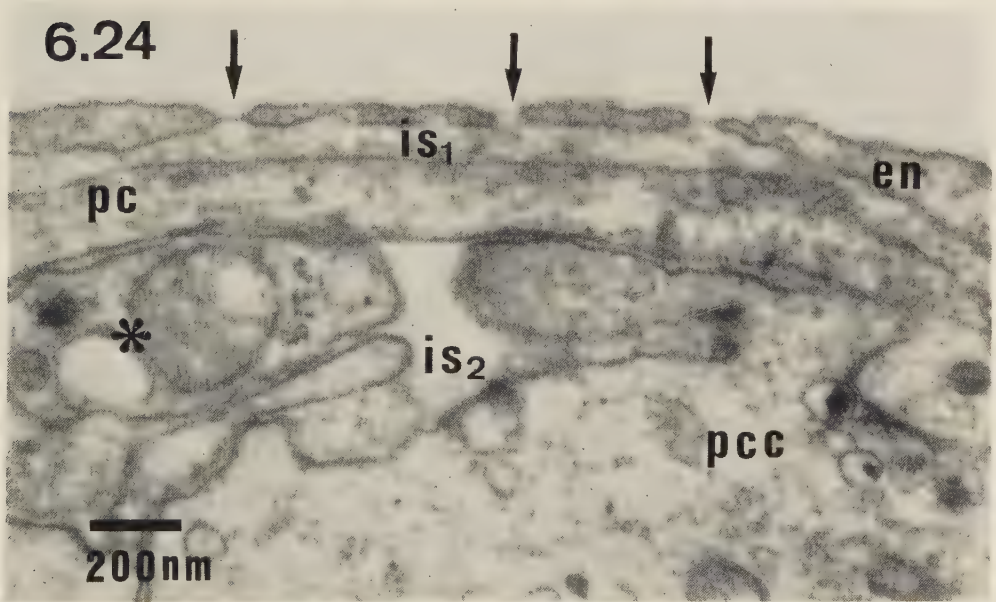
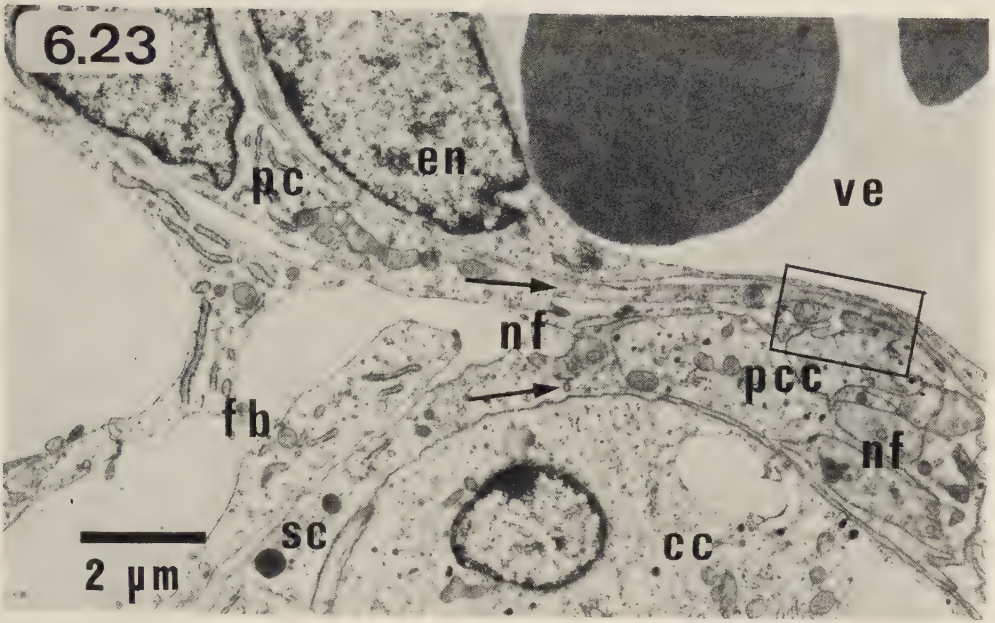


Fig. 6.25.

Vessel. Tympanojugular glomus cr 62a.

The vessel wall (ve) is made up of thin endothelium (en) and a pericyte (pc). Around the vessel chief cells (cc) with pale (cc₂) or dark (cc₁) cytoplasm. The chief cells are partially invested by thin cytoplasmic processes (arrows).

Magnification: $\times 4,500$.

Fig. 6.26.

Relation of glomus cells to endothelium and nerve fibres. Tympanojugular glomus cr 62a.

In short areas the plasma membranes of chief cell parts (cc) adjoining mutually or adjoining nerve fibres (nf), but otherwise they are mainly invested by a supporting cell (sc). Between the supporting cell and the vascular endothelium (en) an irregular perivascular space with cell processes (pc). In this medium magnification the fenestrae (arrows) stand out as patent canals through the endothelium.

Magnification: $\times 19,500$.

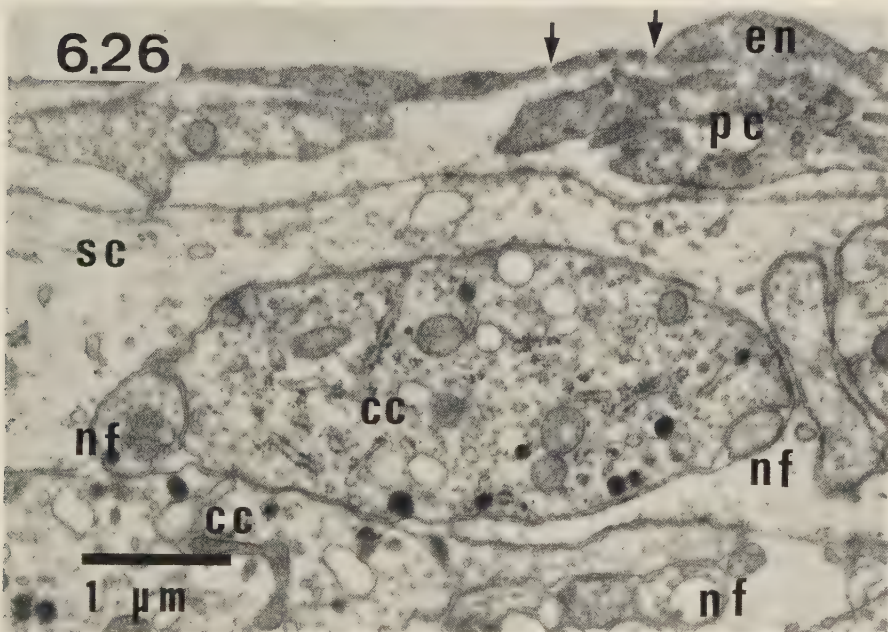
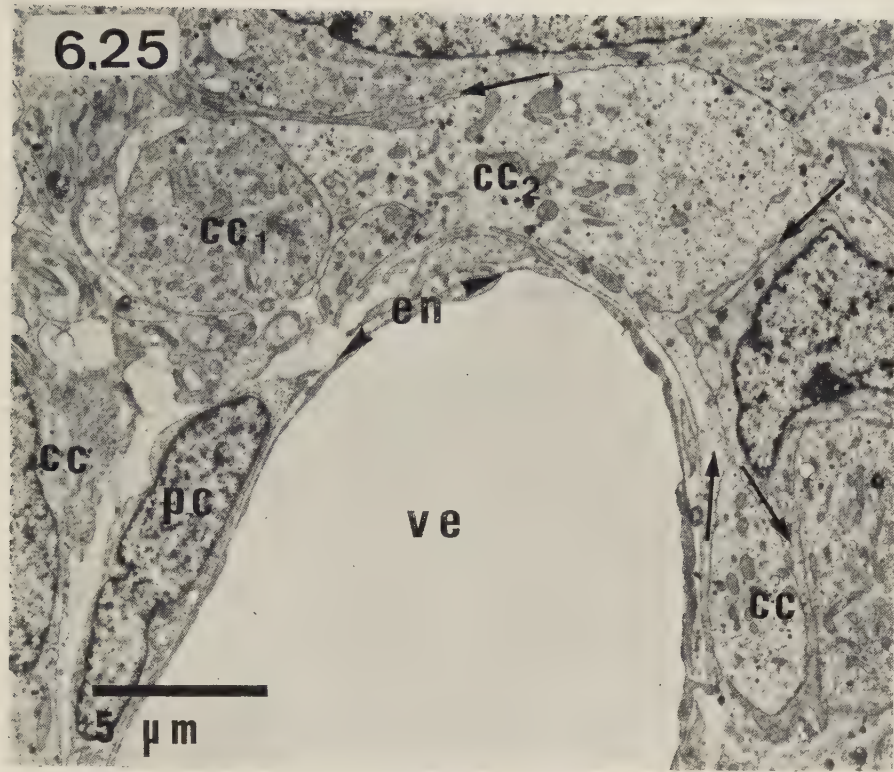


Fig. 6.27.

Chief cell and supporting cell. Tympanojugular glomus cr 59.

In the chief cell (cc) the nucleus (nu) shows a nucleolus (nl) surrounded by chromatin condensations (ch). In the cytoplasm of the supporting cell (sc) granular endoplasmic reticulum (ger), Golgi apparatus (g), and mitochondria (m). The cytoplasm of the supporting cell invests partly the chief cell and partly a group of nerve fibres (nf₂). Between the supporting cell and the chief cell there are in several places interposed very thin cell processes (arrows) whose origin cannot be traced. The chief cell and a chief-cell process (pcc) are in contact with nerve fibres (nf₂). The cells are the same as those illustrated in the area around cc₁ in Fig. 6.20.

Magnification: $\times 11,300$.

6.27

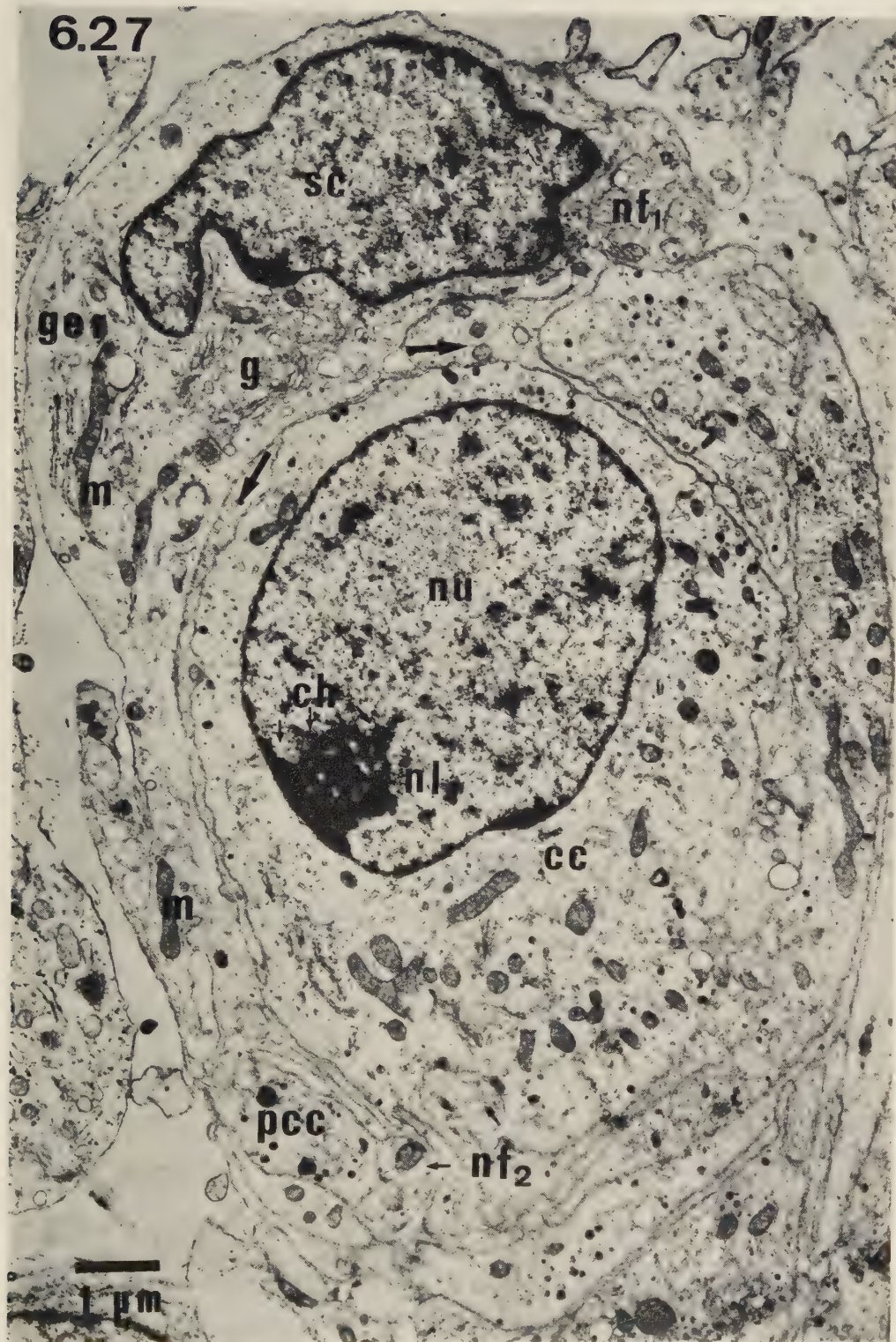


Fig. 6.28.

Electron microscopic low power view. Tympanojugular glomus cr 62d.

Chief cell (cc), chief-cell processes (pcc), and supporting cells (sc) with processes (arrows) situated together with nerve fibres (nf) in the vicinity of a vessel (ve).

Magnification: $\times 5,100$.

Fig. 6.29.

Higher magnification of an area with chief-cell and supporting-cell parts from Fig. 6.28. Tympanojugular glomus cr 62d.

Between the supporting cell (sc) and the chief cells (cc) nerve fibres (nf) are visible. The chief cells are connected by a desmosome (d). In the chief-cell cytoplasm the Golgi zone is distinct (g).

Magnification: $\times 12,800$.

Fig. 6.30.

Detail. Tympanojugular glomus cr 55.

In limited areas of the two chief-cell plasma membranes two desmosome-like structures (d). At the top on the right part of the chief-cell nucleus (nu) whose outer nuclear membrane (at the arrow) herniates into the cytoplasm as agranular endoplasmic reticulum (aer). The perinuclear cistern is closed by a nuclear pore (np).

Magnification: $\times 63,000$.

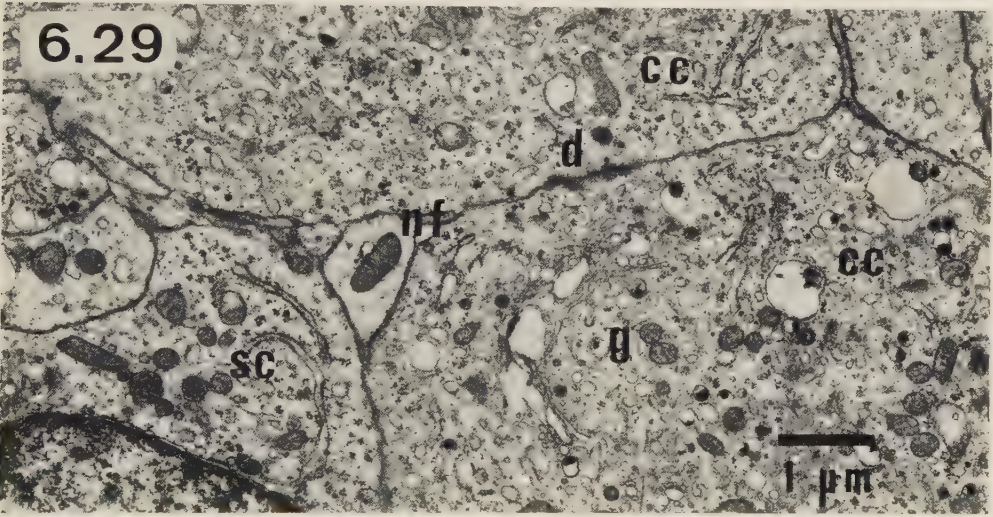
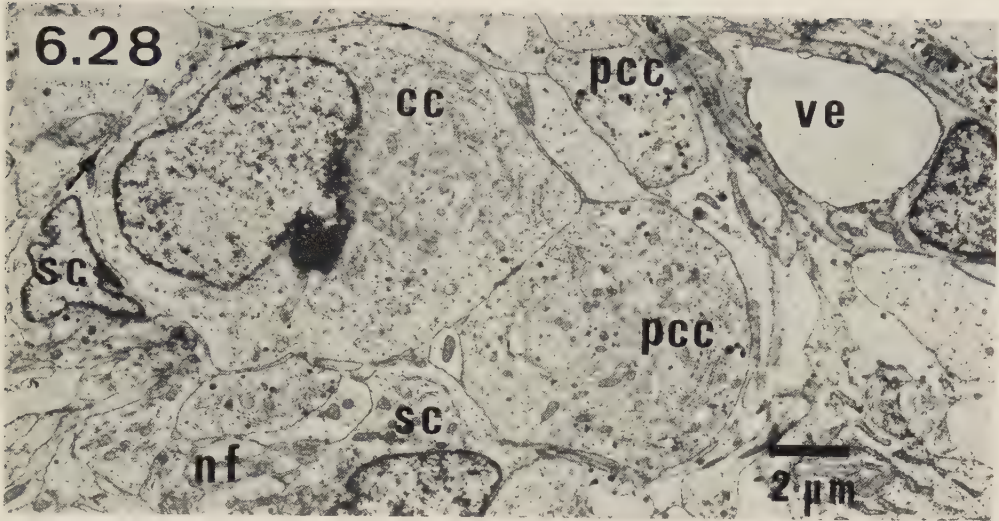


Fig. 6.31.

Organelles in chief cells. Tympanojugular glomus cr 62c.

Medium electron microscopic magnification of the chief cell marked cc_1 in Fig. 6.18. The chromatin in the nucleus of this chief cell is granular and concentrated predominantly in fragments (ch) which are partly scattered in the nuclear ground substance and partly accumulated beneath the nuclear membranes which contain pores (np) in places. In the cytoplasm: Golgi zone (g) whose only cistern contains electron-opaque material of an appearance like the content of the specific granules (sg), mitochondria (m), granular endoplasmic reticulum (ger), vacuoles with pale content (va), electron-opaque body (db), cilium (ci), cf. Fig. 6.32. The plasma membrane of the chief cell runs parallel to the plasma membranes of other chief cells (cc), separated by a narrow intercellular space.

Magnification: $\times 17,800$.

Fig. 6.32.

Detail from Fig. 6.31. Tympanojugular glomus cr 62c.

Cilium (ci) with $9 \times 2+0$ filament structure. The cilium is deeply invaginated in the cell, and it will be noted that the surrounding plasma membrane is coated. Vacuole with pale content (va_1), presumably a Golgi vacuole, cf. Fig. 6.31, vacuole (va_2) of a size like granule vesicles having a content of the same medium electron opacity as the area between the nucleus and the vesicle of the specific granules (sg), ribosomes (r), longitudinally and transversely cut microtubules (mt).

Magnification: $\times 77,000$.

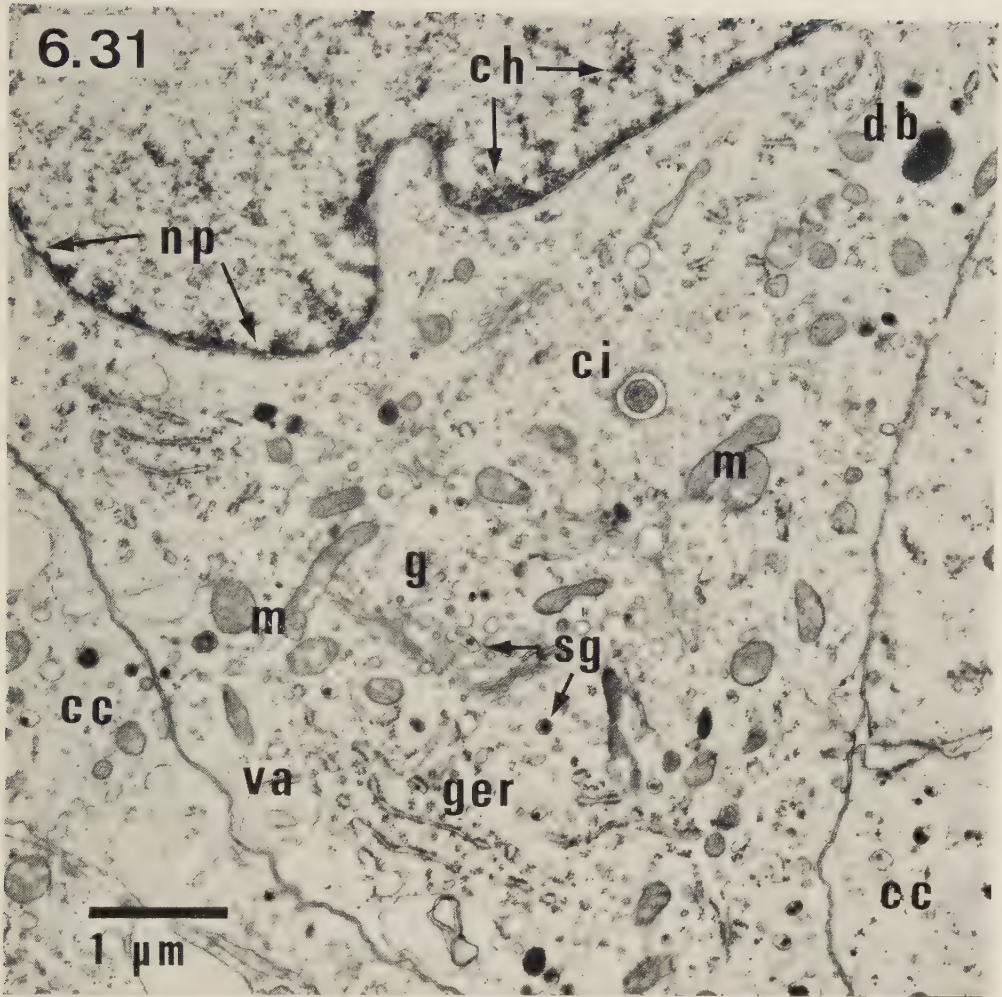


Fig. 6.33.

Organelles in a chief cell. Tympanojugular glomus cr 59.

In the centrosome a transversely cut centriole (ce) and stacks of Golgi lamellae (g). The cisterns belonging to the granular endoplasmic reticulum (ger) are situated peripherally in the cell. Specific granules (sg), mitochondria (m), agranular vacuoles with pale content (va), microtubules (mt), vesicle-containing body (vcb).

Magnification: $\times 20,000$.

Fig. 6.34.

Golgi zone and specific granules in a chief cell. Tympanojugular glomus cr 59.

The Golgi zone (g) is built up of three to four layers of curved, parallel cisterns whose contents are somewhat more electron-dense and structured than the cytoplasmic ground substance. Terminally in a cistern (thick arrow) the content is of the same electron density as the core of the specific granules (sg_1). Around a Golgi cistern small vesicles (vs), vacuoles (va), whose size corresponds to the vesicle in the specific granules (sg_3), and free as well as membrane-bound ribosomes (r). The structure of a specific granule contains an electron-dense core (sg_1) ill-defined from the surrounding paler corona (sg_2). The latter is well-defined from the surrounding ground substance of a unit membrane (sg_3).

Magnification: $\times 73,500$.

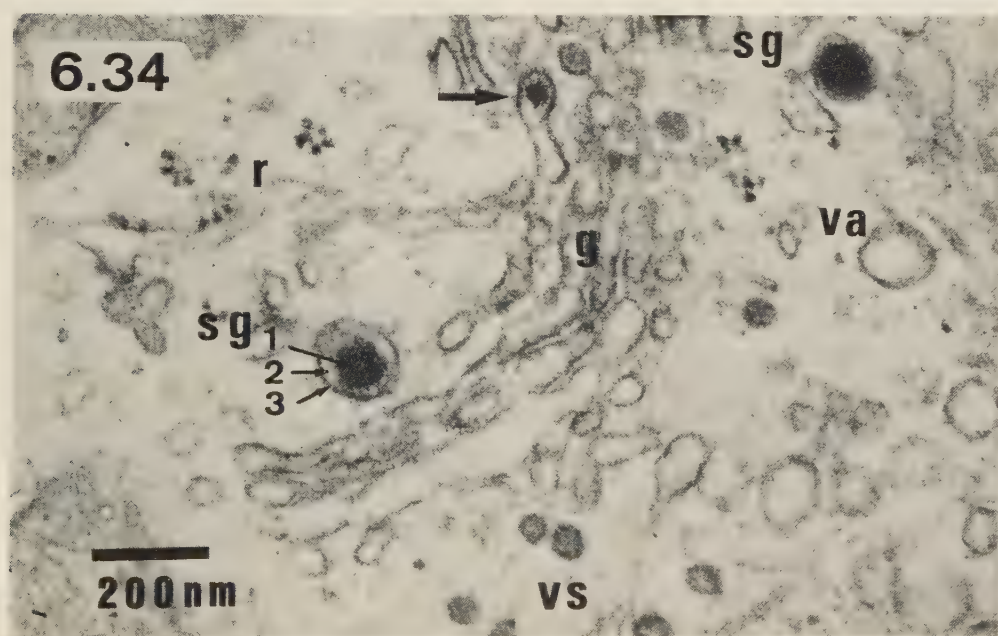
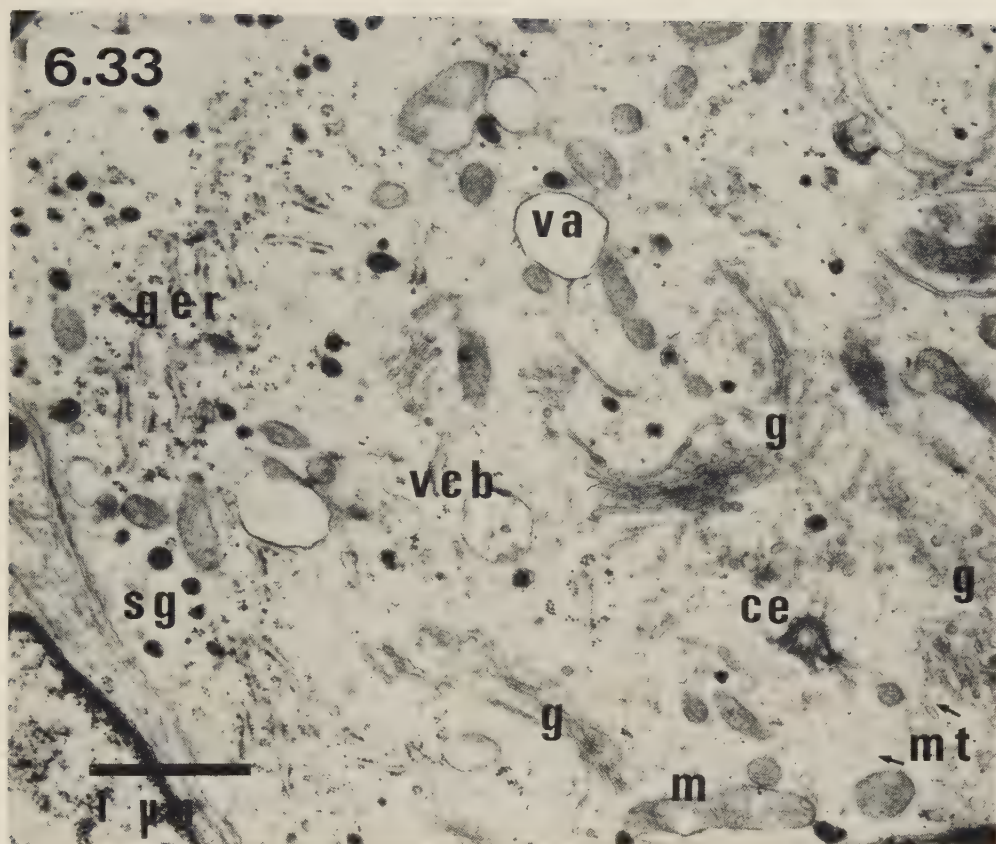


Fig. 6.35.

Detail of a chief cell. Tympanojugular glomus cr 62f.

The Golgi zone (g) is predominated by vesicles and vacuoles. Mitochondrion with mitochondrial granules (arrows), membrane-bound body containing small vesicles (vcb), ribosomes bound to membranes (ger), ribosomes lying free in the cytoplasmic ground substance, arranged in rosettes (r), specific granules (sg).

Magnification: $\times 65,600$.

Fig. 6.36.

Detail. Tympanojugular glomus cr 62c.

The plasma membranes between two granular chief cells (sg) are joined by a longish desmosome (d). At the place of contact between a chief cell and nerve fibres (nf), on the other hand, no membrane specialisations. Insert: A specific granule (sg₂) magnified so that the trilaminar structure of the vesicular membrane is visible (between the arrows).

Magnification: $\times 48,500$. Insert: $\times 114,000$.

Fig. 6.37.

Centriole in a chief cell. Tympanojugular glomus cr 62c.

The centriole (ce) is a little obliquely cut, so that only six of the triplets are visible. In the satellites of the centriole microtubules (arrows) are anchored.

Magnification: $\times 62,700$.

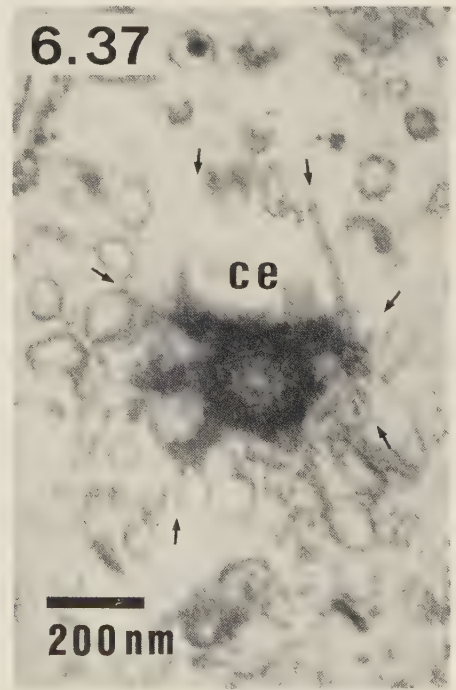
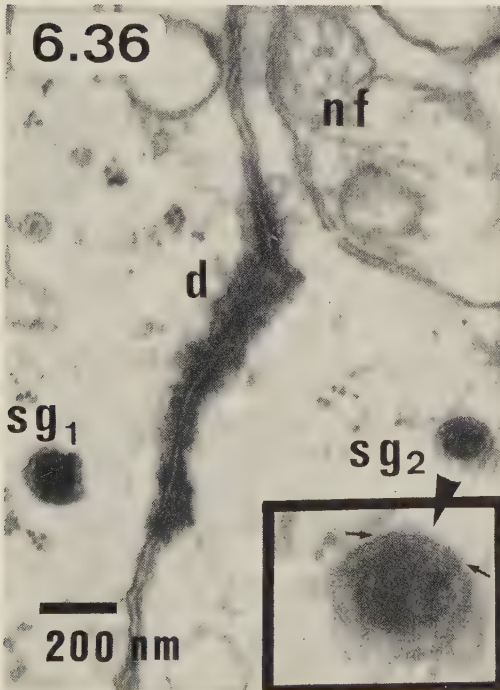
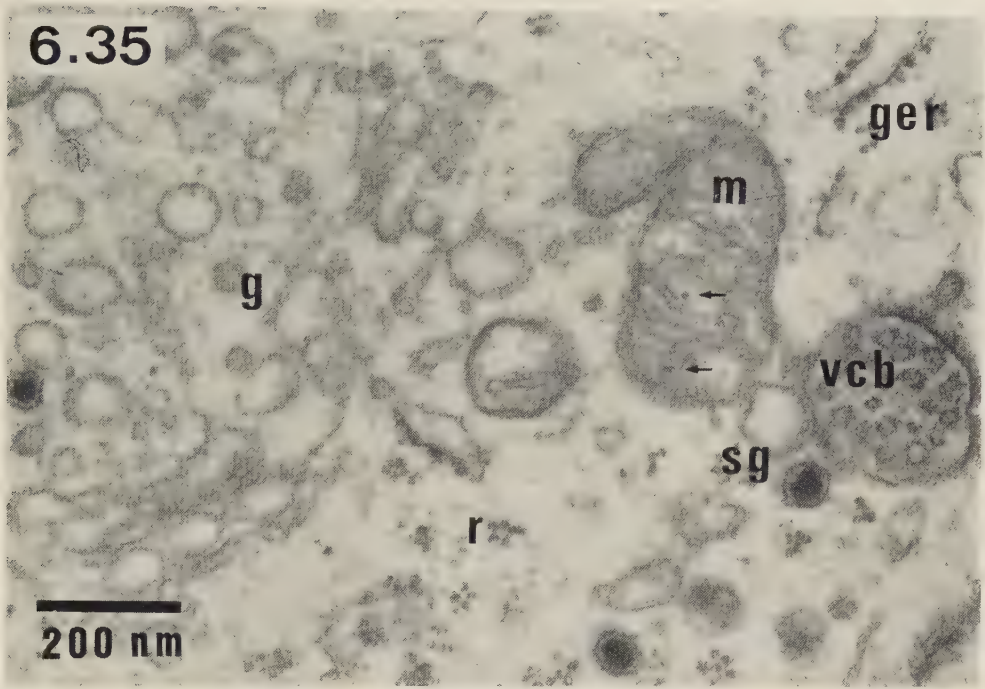


Fig. 6.38.

Detail of chief cells. Tympanojugular glomus cr 59.

Desmosome-like contact (d) between the plasma membranes of chief cells, agranular endoplasmic reticulum (aer), but possibly with one attached ribosome (arrow), solitary free ribosomes (r), mitochondrion (m), specific granules (sg).

Magnification: $\times 77,000$.

Fig. 6.39.

Detail at site of contact between glomus cells and nerve fibres. Tympanojugular glomus cr 59.

Partially embedded in a supporting cell (sc), but adjoining a chief cell (cc) two transversely cut nerve fibres (nf) with neurotubules (nt). Granules in the chief cell show quite marked variation in size and appearance, a variation which may be due partly to some granules being cut close to the centre (sg_1), others peripheral to the centre (sg_2). Micropinocytotic coated vesicle (mpv) in continuity with the plasma membrane.

Magnification: $\times 45,800$.

Fig. 6.40.

Detail of chief-cell process. Tympanojugular glomus cr 62a.

Specific granules (sg) a few of which apparently contain a double core (sg_0), numerous longitudinally cut microtubules (mt), and mitochondrion (m).

Magnification: $\times 54,200$.

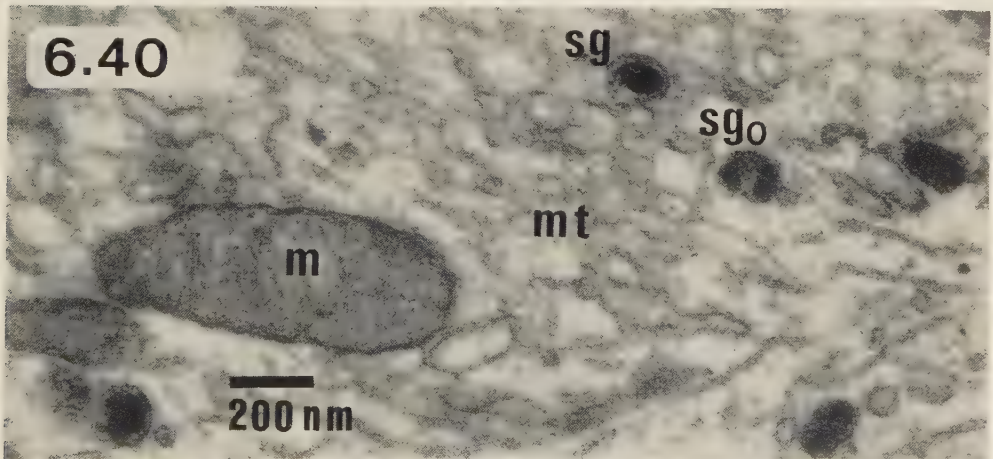
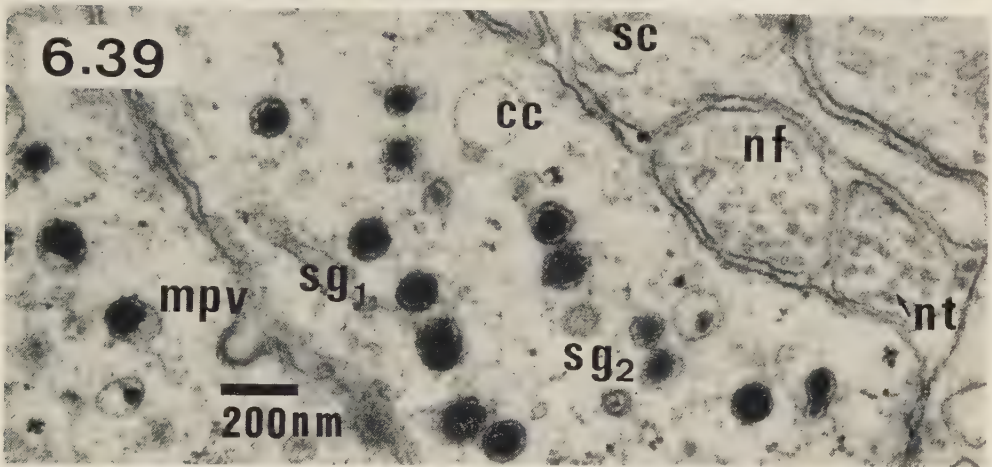
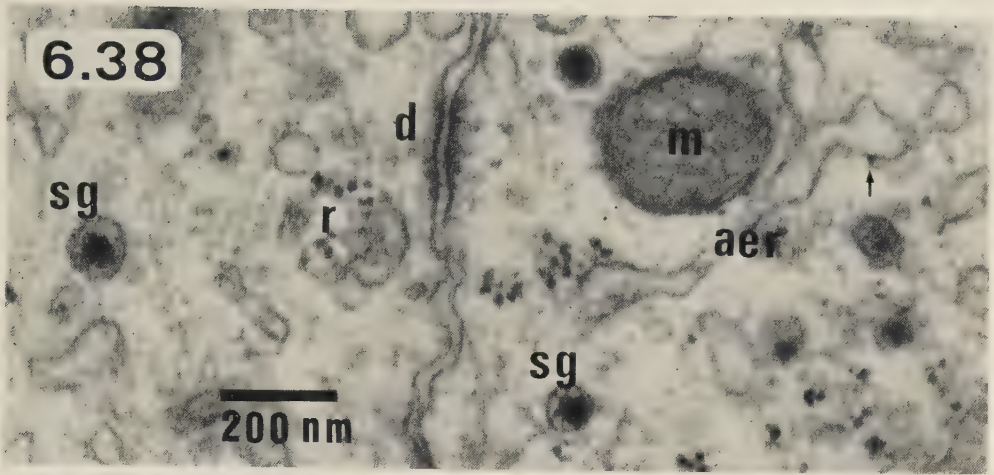


Fig. 7.1.

Light microscopic low power view. Vagal glomus cr 62.

Survey section showing a glomus (1) in the juxtavagal position at the surface of the inferior vagal ganglion at the junction between the ganglion cells (2) and the peripheral nerve trunk (3).

Magnification: $\times 160$.

1. Vagal glomus.
2. Ganglion cells.
3. Vagus trunk.

Fig. 7.2.

Light microscopic micrograph. Vagal glomus cr 62.

At this magnification of the glomus marked 1 in Fig. 7.1 a distinction may be made between vascular cells, viz. endothelial cells (2) and pericytes (3), and glomus cells, viz. chief cells (5) and supporting cells (4).

Magnification: $\times 640$.

1. Vessel.
2. Endothelial cell.
3. Pericyte.
4. Supporting cell.
5. Chief cell.

Fig. 7.3.

Light microscopic micrograph. Vagal glomus cr 59b.

In this section the glomus is divided into two lobes (1). It is situated in loose, vascular mesenchyme between axon bundles (2) and ganglion cells (3). In one site the glomus adjoins axon bundles (2₁), but otherwise it is delimited from the mesenchyme mainly by vessels (4). The predominant type of cell in the glomus has regularly shaped nuclei of a delicate chromatin structure and ample, pale cytoplasm.

Magnification: $\times 640$.

1. Glomus.
2. Axon bundles.
3. Ganglion cells.
4. Vessel.

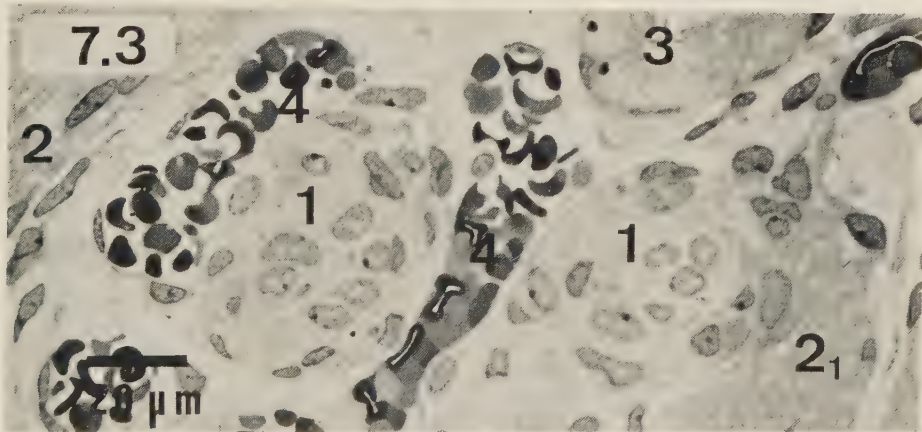
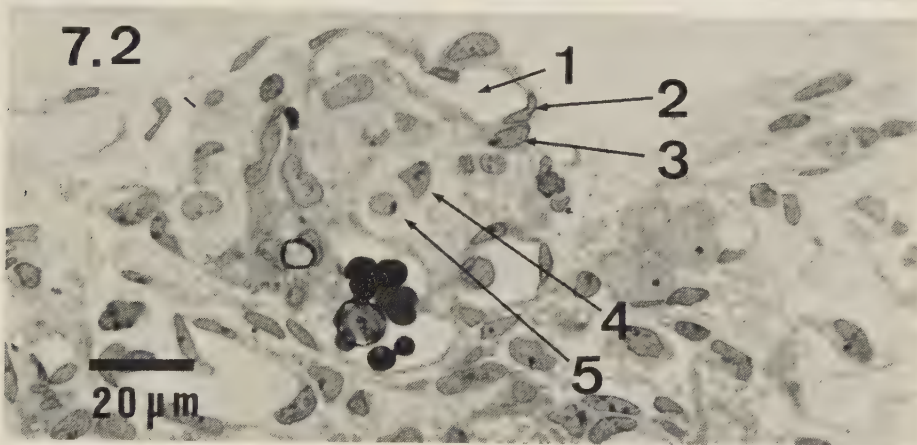
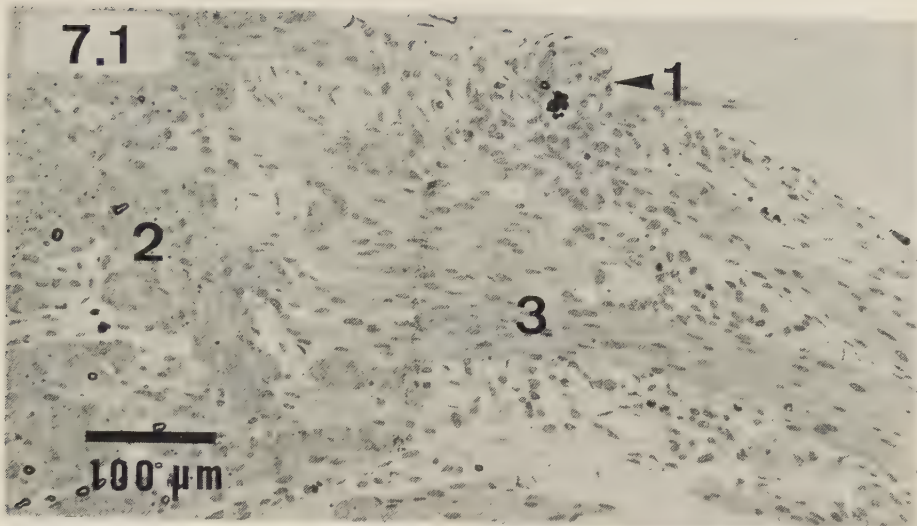


Fig. 7.4.

Light microscopic micrograph. Vagal glomus cr 55a.

Survey section from the peripheral part of the inferior vagal ganglion. In the mesenchyme between the ganglionic nerve fibres (4) and the ganglion cells (3), a group of glomus cells (1) which – except for a short pedicle to the mesenchyme – are completely enveloped by a vascular lumen (2).

Magnification: $\times 640$.

1. Glomus cells.
2. Vascular lumen.
3. Ganglion cells.
4. Bundle of nerve fibres.

Fig. 7.5.

Electron microscopic low power view. Vagal glomus cr 55b.

Electron microscopy reveals an intricate mutual relation between the cells (asterisks). The rounded nuclei belong to chief cells (cc). Already at this magnification the cytoplasm may be seen to be studded with small, deeply staining granules and to contain mitochondria and pale vacuoles. The cytoplasm of the cells exhibits some variation in electron opacity (cf. cc_1 and cc_2). The banana-shaped nucleus with nucleolus and the deeply notched nucleus presumably belong to supporting cells (sc)

Magnification: $\times 2,800$.

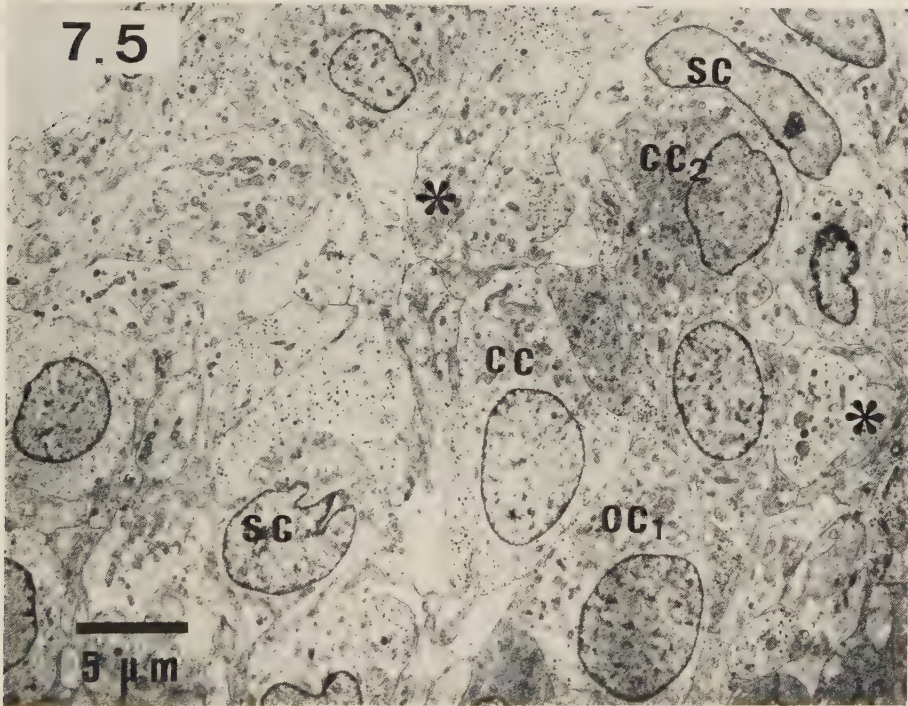
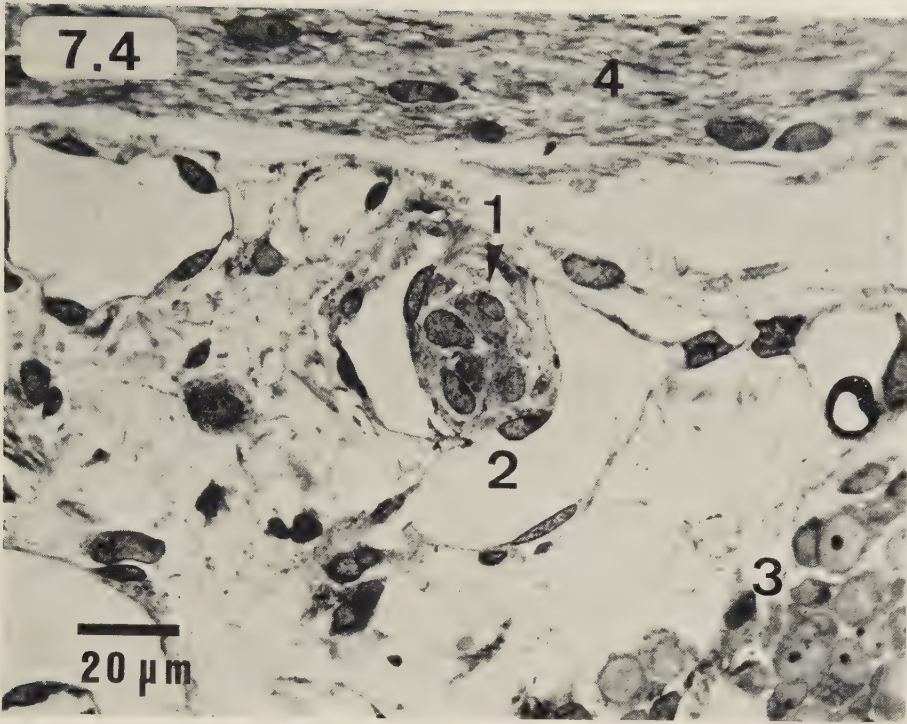


Fig. 7.6.

Electron microscopic low power view. Vagal glomus cr 59a.

The group of cells consists of granular chief cells (cc) and a non-granular supporting cell (sc) whose nucleus is deeply notched at the site of a granular cell process (arrow). The area between the chief cells marked cc is of a complicated structure showing numerous cell processes, a few of which can be identified, in this magnification, as longitudinally and transversely cut chief-cell processes (pcc) and nerve fibres (nf). Around the group of cells connective tissue (ct), axon bundles (nc), and thin-walled vessels (ve), partially invested by perivascular cells (pc).

Magnification: $\times 4,600$.

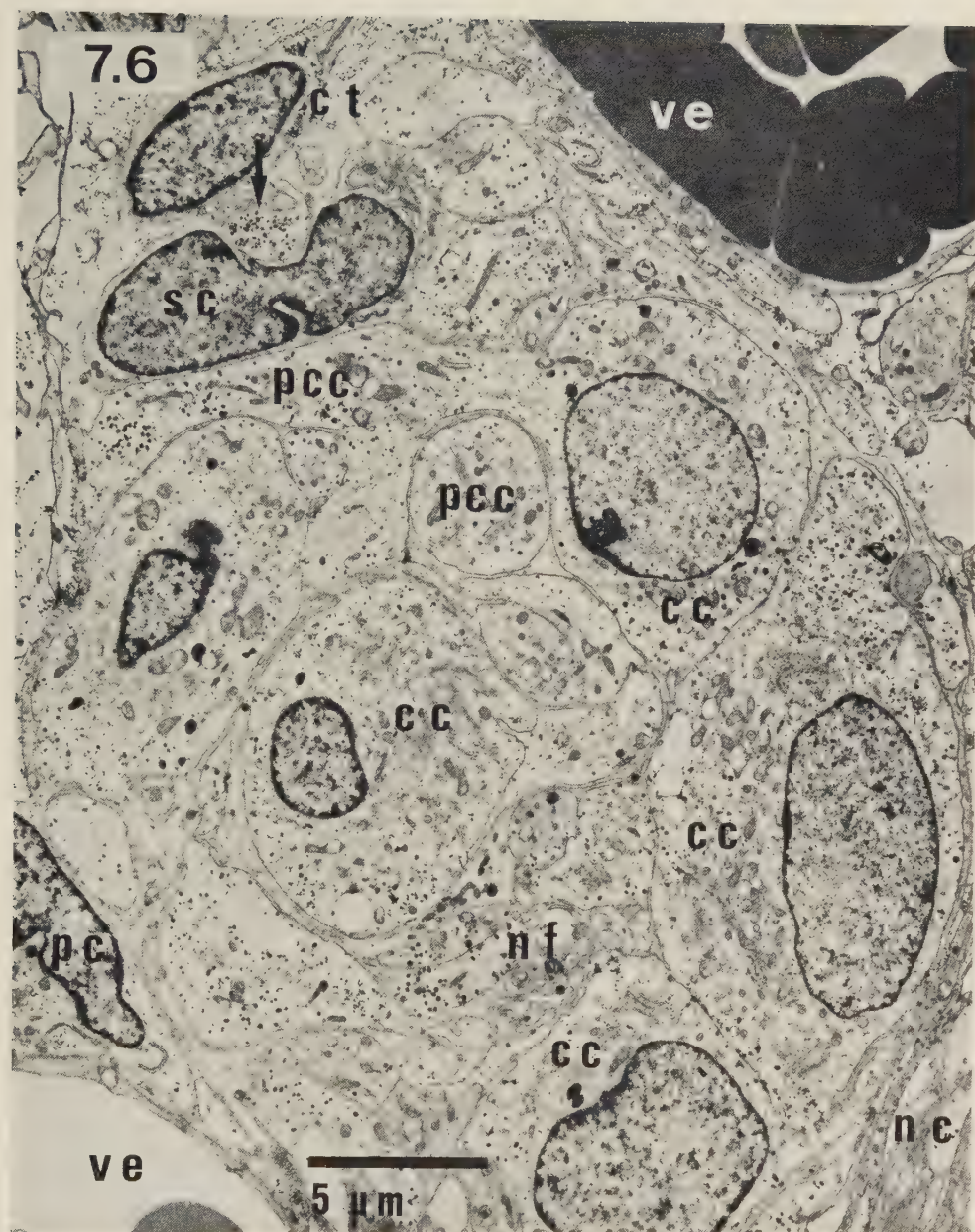


Fig. 7.7.

Medium electron microscopic magnification of a supporting cell. Vagal glomus cr 62.

In this section the nucleus of the supporting cell (sc) is triangular and notched (at nf_1 and nf_2). The chromatin is concentrated immediately beneath the nuclear membrane, forming central to this discrete accumulations in the pale nuclear ground substance. The two membranes of the perinuclear cistern (ne) may be discerned. The juxtannuclear cytoplasm is scanty and contains a few mitochondria (m) and free and membrane-bound ribosomes (r). The plasma membrane of the supporting cell adjoins chief cells (cc), nerve fibres (nf), and non-granular cell processes (psc).

Magnification: $\times 15,700$.

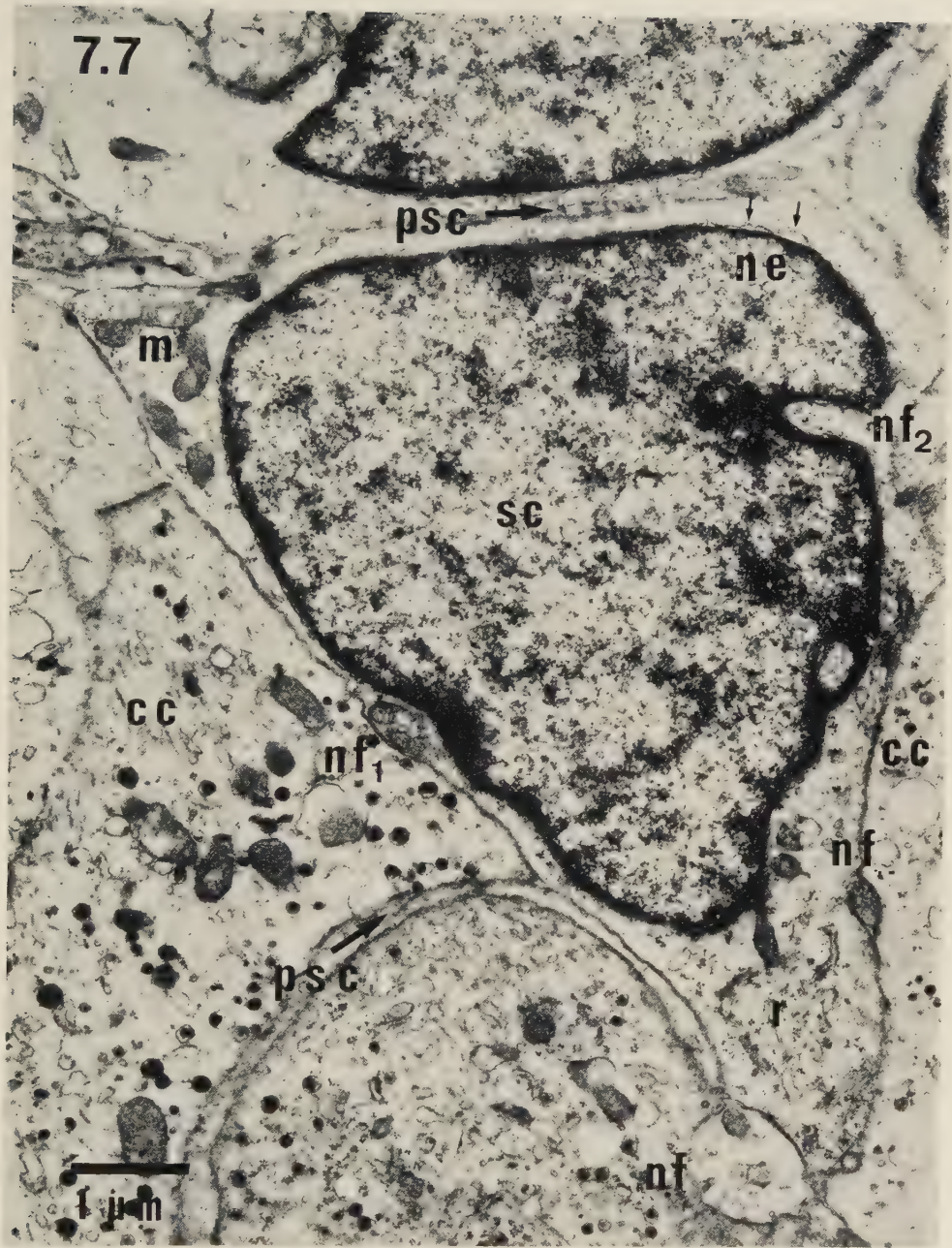


Fig. 7.8.

Electron microscopic low power view showing the relationship between chief cells and supporting cells. Vagal glomus cr 59a.

The chief cell (cc) is invested by supporting cells (sc), supporting-cell processes (arrows), and part of another chief cell (1). Between the latter and other chief-cell parts (2, 3, 4) a bundle of nerve fibres (nf) is interposed. The structure marked 5 is given in higher magnification in Fig. 7.17.

Magnification: $\times 7,600$.

Fig. 7.9.

Organelles in a juxtannuclear area of a chief cell. Vagal glomus cr 59a.

The predominant structures in the cytoplasm are the Golgi zone (g), mitochondria (m), and osmiophilic granules (sg). The endoplasmic reticulum (er), whose membranes are in short areas studded with ribosomes, is less predominant. Ribosomes are present also without relation to membranes, partly as solitary particles and partly in rosette-like groups (r). In addition, a few microtubules (mt) and pale vacuoles (va), one of which (va₁) is a dilated mitochondrion. The chief cell is enveloped by a supporting-cell process (psc) and an interstice of collagen fibres (cf).

Magnification: $\times 33,000$.

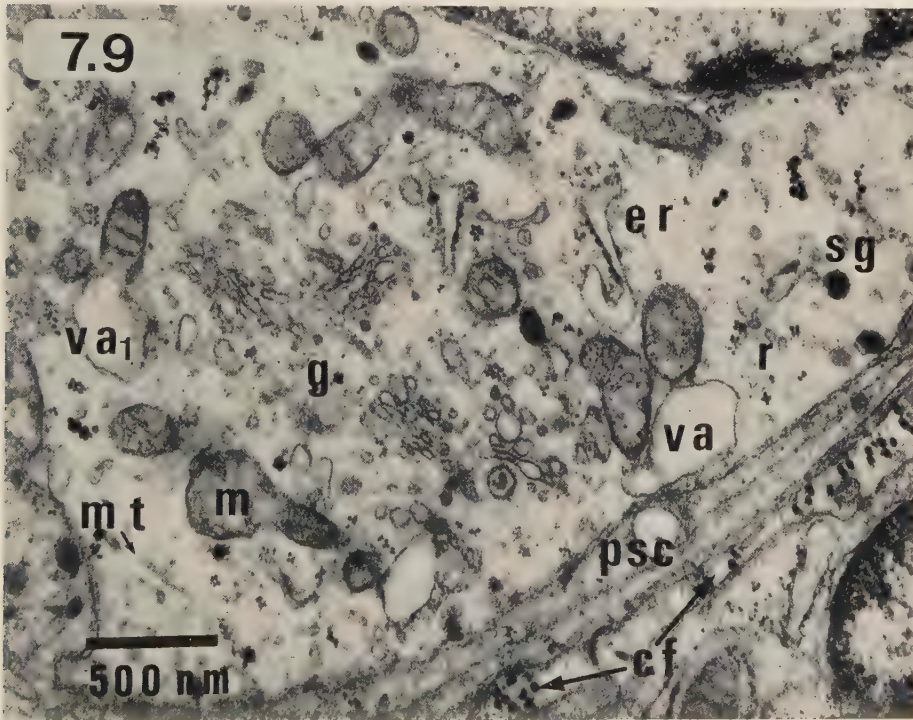
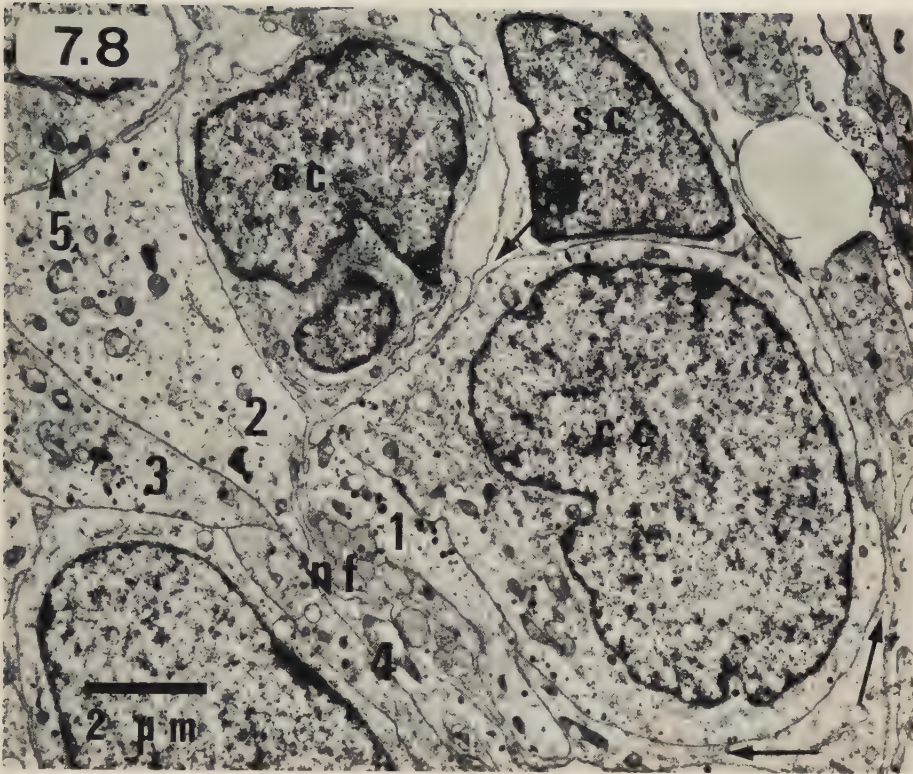


Fig. 7.10.

Organelles in a chief cell. Vagal glomus cr-55b.

In the sectioning the Golgi apparatus (g) has been hit so that it appears as a horseshoe-shaped, concentric layer of cisterns (1) embracing vacuoles (2) and numerous vesicles (3). The rough endoplasmic reticulum (ger) forms a stack of 6 ribosome-studded cisterns. In addition, the cell contains a lysosome-like body in the form of a multi-vesicular body (vcb) and a dense body (db).

Magnification: $\times 30,000$.

Fig. 7.11.

Detail of Golgi zone. Vagal glomus cr 59b.

In the interior of a Golgi cistern (g) two rounded bodies (large arrows) of the same homogeneous, electron-opaque appearance as the cores of the specific granules (sg). Between the two bodies the Golgi membrane undulates (small arrows). This finding might indicate that the vesicles of the specific granules are buddings from the membrane systems of the Golgi apparatus.

Magnification: $\times 75,500$.

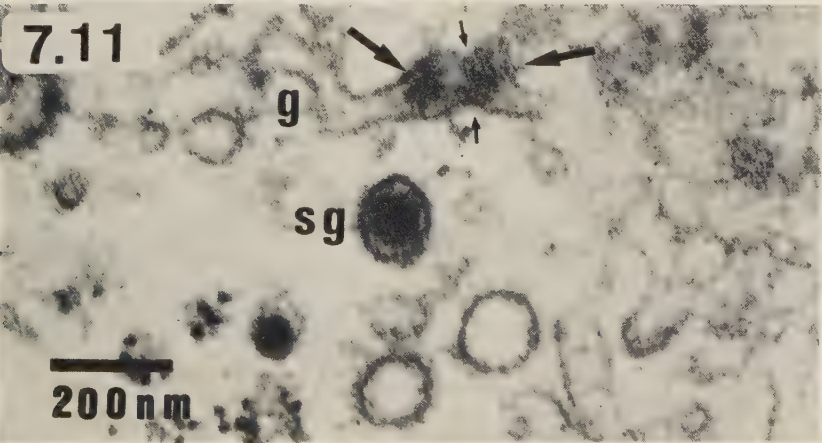
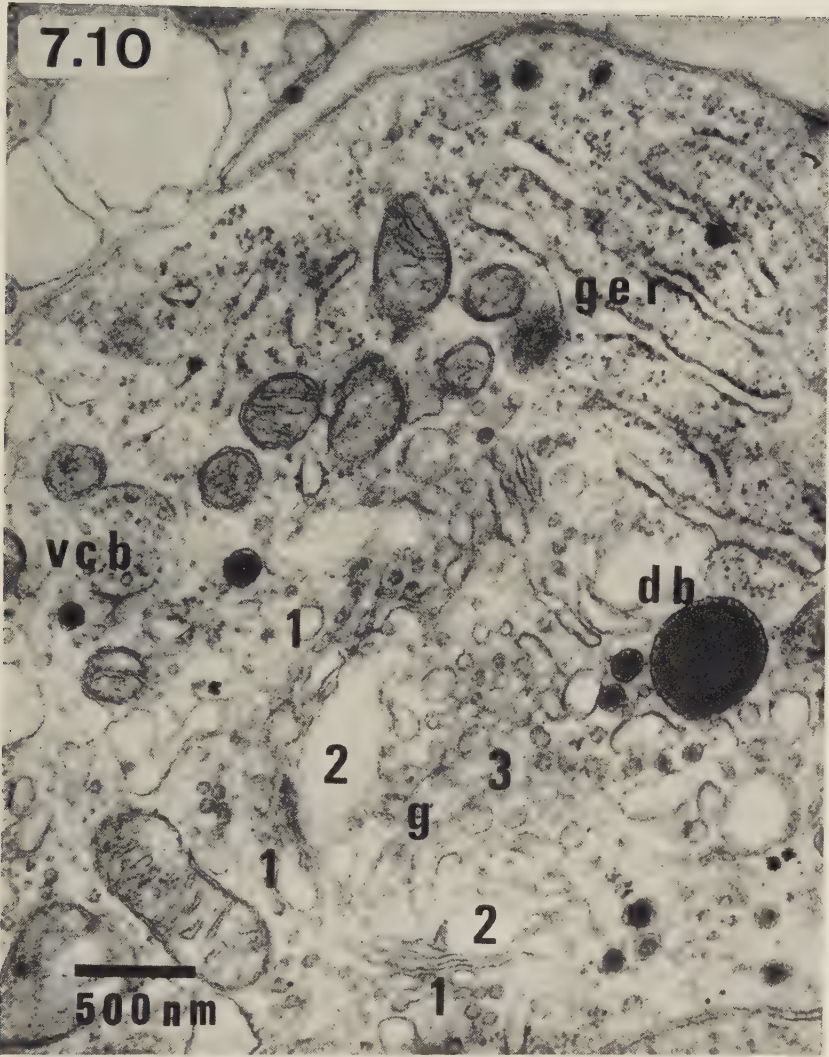


Fig. 7.12.

Relations of nerve fibres. Vagal glomus cr 55b.

By way of mesaxons (mx) the intercellular space between the chief cell (cc) and the supporting cell (sc) communicates with the space surrounding the nerve fibres (nf). In the axoplasm there are mitochondria (m), vacuoles (va), and numerous neurotubules (nt).

Magnification: $\times 40,500$.

Fig. 7.13.

Chief-cell processes. Vagal glomus cr 55b.

A chief-cell process (pcc) contains small mitochondria (m), pale vacuoles (va), and microtubules (mt). The processes are distinguishable from the nerve fibres (cf. Fig. 7.12) only if the section contains specific granules (sg).

Magnification: $\times 40,500$.

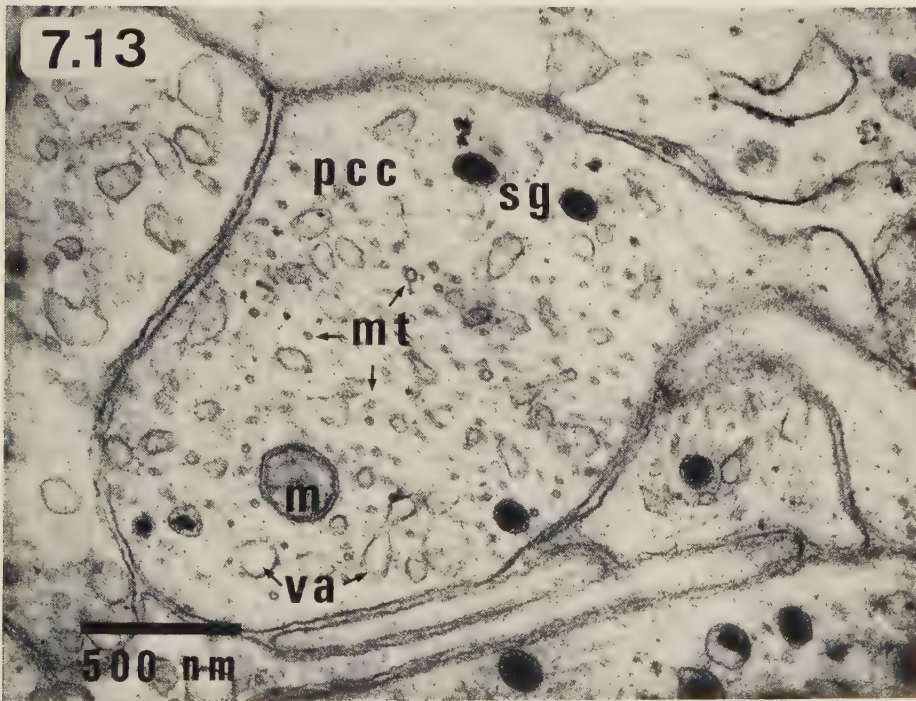
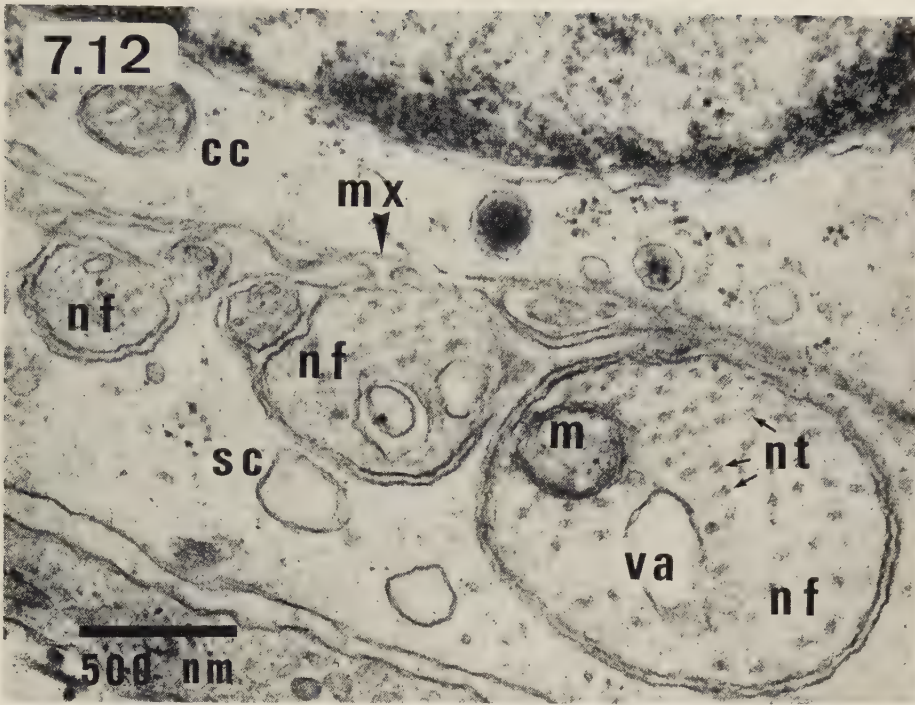


Fig. 7.14.

Relationship between chief cell and vessel. Vagal glomus cr 59b.

Between the vascular lumen (lu) and the chief cell (cc) a supporting-cell process (sc), a connective-tissue space with longitudinally and transversely cut collagen fibres (cf), a cytoplasmic process (pc), a perivascular, amorphous area containing an extravasated part of a red blood cell (rbc) and endothelium (en) with a number of membrane-closed fenestrae (ep).

Magnification: $\times 57,000$.

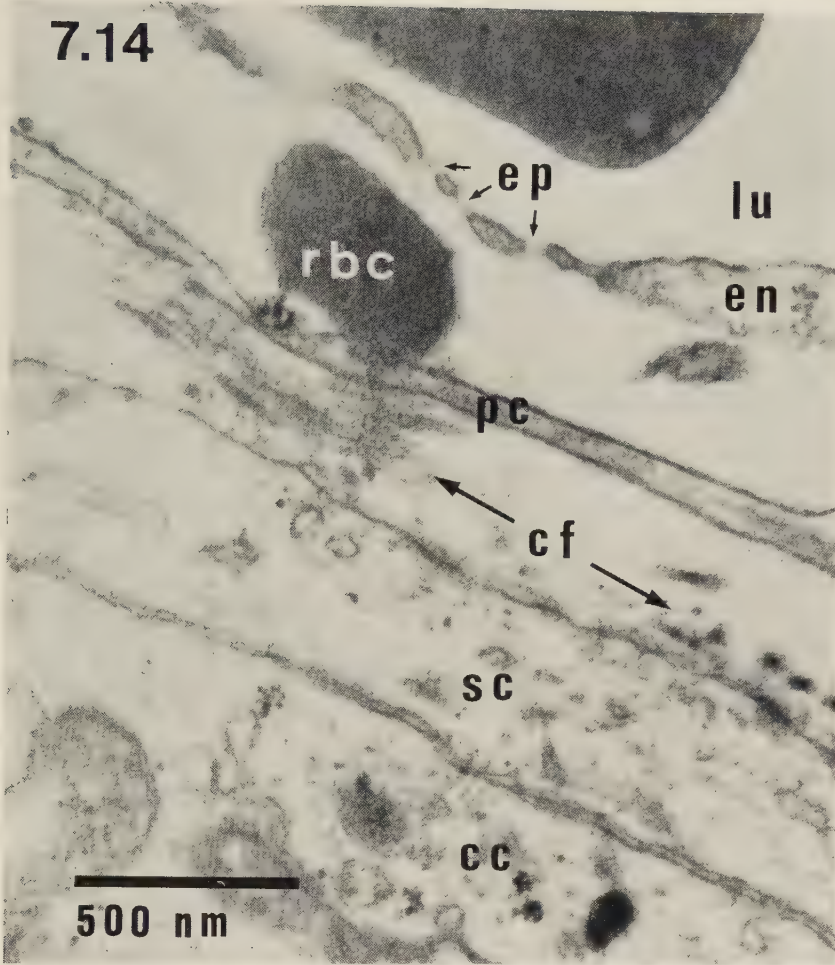
Fig. 7.15.

Relationship between chief cell and vessel. Vagal glomus cr 55b.

Between the chief cell part (cc) and the vascular lumen (lu) there is, apart from the endothelium (en) only an irregular interstice (is). The endothelium contains a micropinocytotic vesicle (mpv) and possibly a fenestra (ep).

Magnification: $\times 45,000$.

7.14



7.15

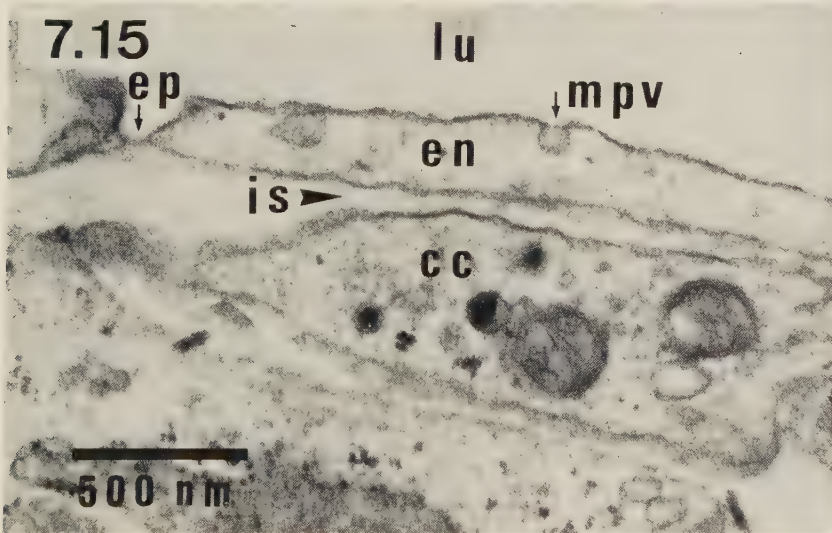


Fig. 7.16.

Detail of chief cell. Vagal glomus cr 59a. .

Plasma membranes of two chief cells of almost parallel course. In the largest areas un-specialized contact with an intercellular interstice (is) of about 15 nm. In a short area the submembranous density characteristic of desmosomes (d). The specific granules (sg) exhibit morphological variation. In addition to typical granules (sg₁) there are granules of an appearance which may be explained by the traumatization of the osmiophilic core (sg₂) or by dilatation of the vesicular membrane (sg₃). Apparently, a vesicle may contain two cores (sg₁). However, this phenomenon may be due to the membrane between two densely lying granules having been sectioned so obliquely that the membranes are not visualized, as is evident e.g. in another granule (sg₅, arrows). At this magnification it is clear that the ribosomes are partly membrane-bound (r₁), partly solitary (r₂), and partly arranged in groups (r₃).

Magnification: $\times 75,500$.

Fig. 7.17.

Detail of chief cell (cf. Fig. 7.8). Vagal glomus cr 59a.

The Golgi zone (g) and an oblique section through a cilium (ci) invaginated in the cytoplasm predominate. The cilium contains 9 pairs of peripheral tubules. Ribosomes (r) are bound to the outer nuclear membrane.

Magnification: $\times 57,000$.

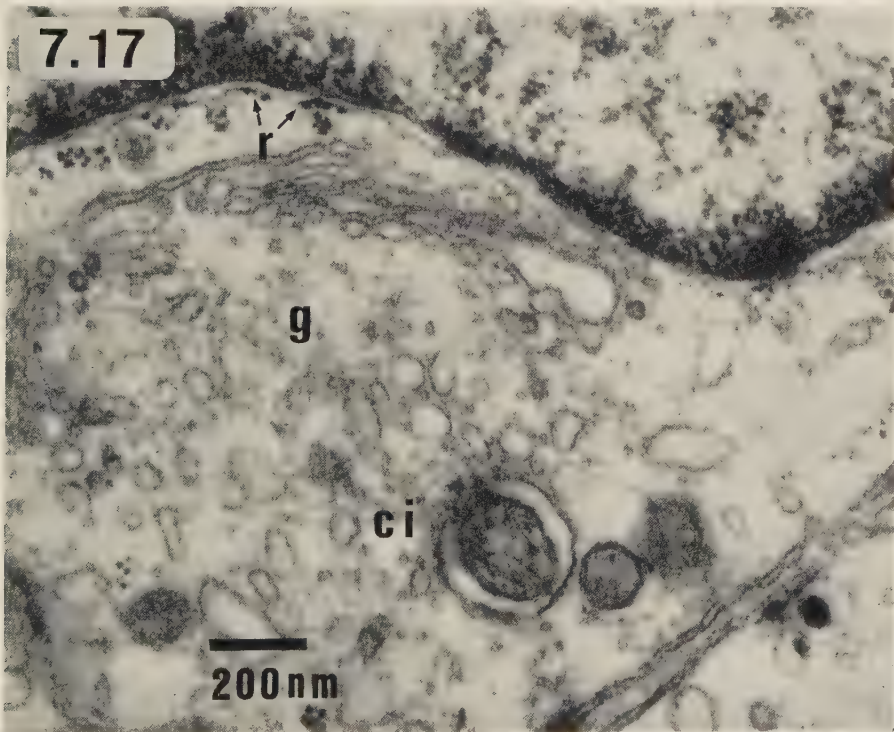
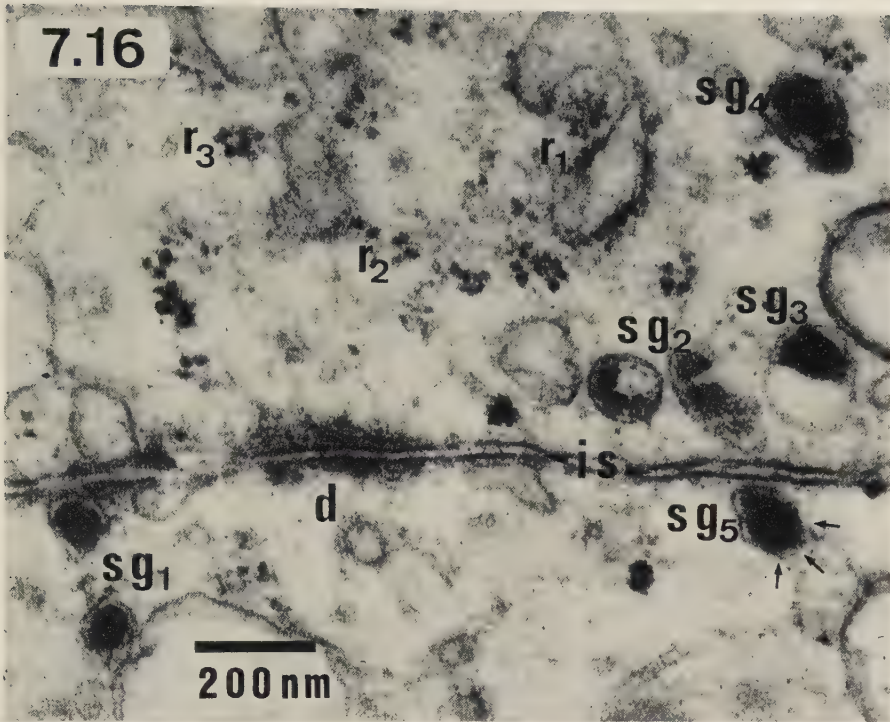


Fig. 7.18.

Contact between chief cell and nerve fibres. Vagal glomus cr 55a.

No accumulation of organelles or membrane specialization at the site of contact between the nerve fibres (nf) and the chief cell (cc).

Magnification: $\times 51,300$.

Fig. 7.19.

Desmosomes. Vagal glomus cr 55a.

Series of desmosome-like (d-d) structures on chief-cell plasma membranes. Agranular endoplasmic reticulum (aer). Nuclear pores (np).

Magnification: $\times 42,000$.

Fig. 7.20.

Specific granules. Vagal glomus cr 62.

A typical granule (sg_1) containing an electron-opaque nuclear area and around it a concentric pale ring delimited by a trilaminar (arrow) membrane. In other granules there is an appearance of dilatation of the vesicular membrane (sg_2) and partial breakdown of the peripheral nuclear material (sg_3). Other structures (sg_4) in this picture are tangentially cut pieces of specific granules.

Magnification: $\times 114,000$.

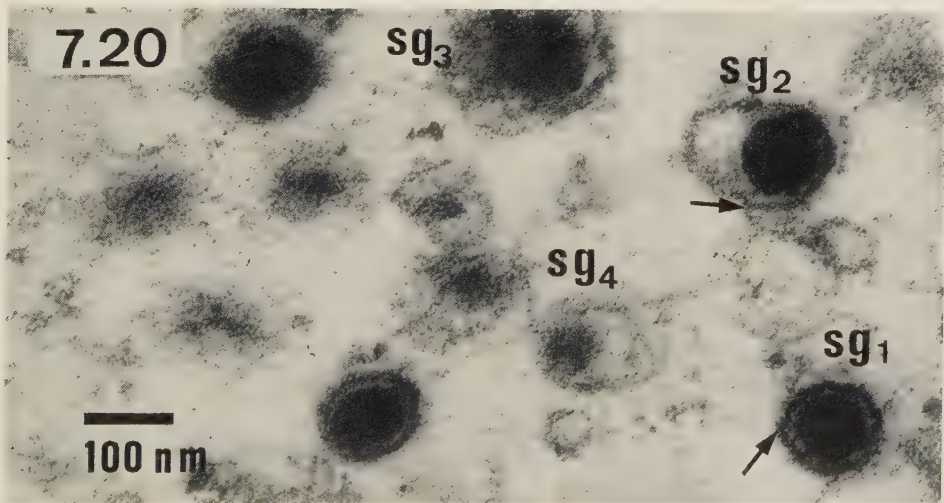
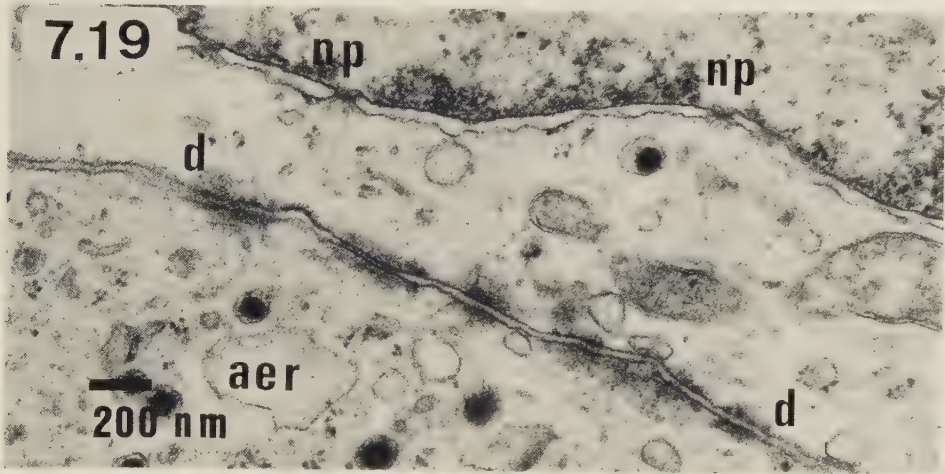
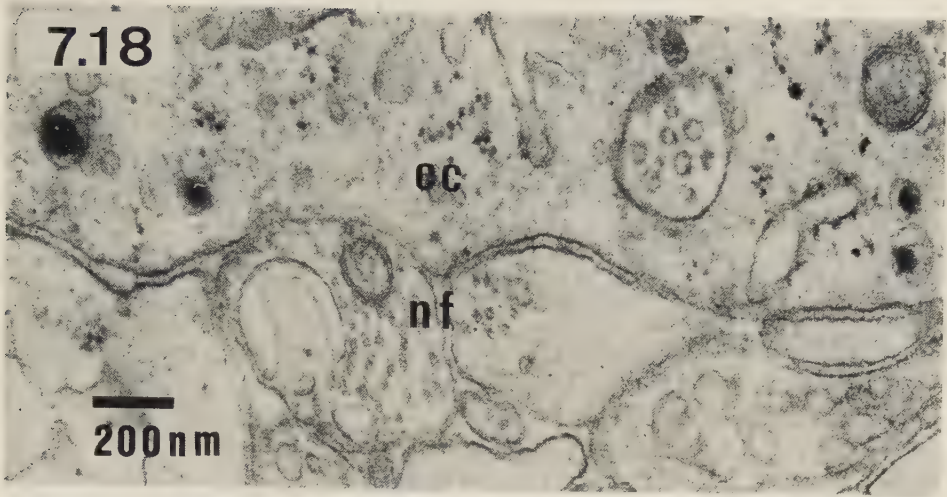


Fig. 9.1.

Light microscopic micrograph. Organ of Zuckerkandl cr 62.

The chromaffin cells (1) are lying as a uniform, compact mass only interrupted by vascular lumina (2). The cytoplasm contains numerous deeply staining granules (arrows) about $0.2\ \mu\text{m}$ in diameter.

Magnification: $\times 640$.

1. Chromaffin cells.

2. Vessels.

Arrows: Granules.

Fig. 9.2.

Electron microscopic low power view. Organ of Zuckerkandl cr 55.

The chromaffin cells are lying in close relation to each other and to the endothelium around vascular lumina (ve). In several cells there is a fairly dark perikaryon predominated by series of granular endoplasmic reticulum (1) and in some of them Golgi complex (2) as well as pale, more peripheral cytoplasmic areas containing punctate granules (glycogen particles), and (3) larger granules showing high contrast (secretory granules, 4). In addition, mitochondria (5) and pale vacuoles (6).

Magnification: $\times 4,500$.

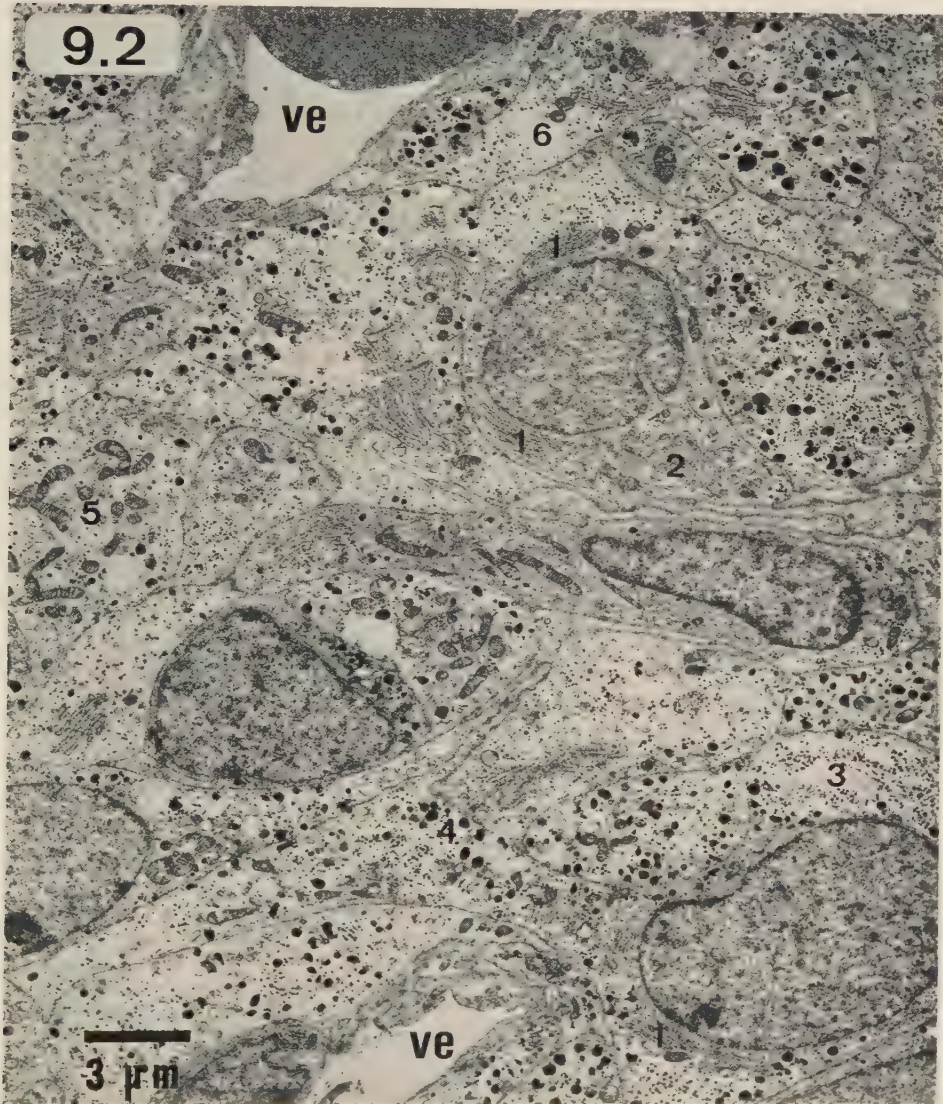
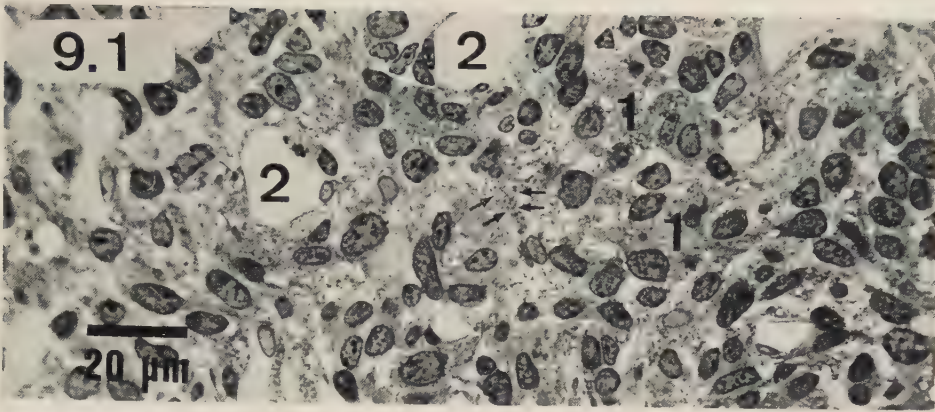


Fig. 9.3.

Typical organelles in a chromaffin cell. Organ of Zuckerkandl cr 55.

Nucleus (nu), granular endoplasmic reticulum (ger), Golgi complex (g), mitochondria (m), vacuoles (va), glycogen (gl), secretory granules (sg).

Magnification: $\times 12,100$.

Fig. 9.4.

Detail from a chromaffin cell. Organ of Zuckerkandl cr 55.

On the left part of a mitochondrion (m) with two mitochondrial granules and the terminal endings of a stack of cisterns from the endoplasmic reticulum, studded with ribosomes (r). Ribosomes are seen also free in the cytoplasm in the vicinity of reticulum. In the surrounding cytoplasmic ground substance there are particles (gl) which in size, electron opacity, and arrangement differ from ribosomes in a way which morphologically characterizes them as glycogen particles in an alpha configuration. Secretory granules are seen in at least two types, partly vesicles with a homogeneous, electron-opaque content (1, 3, 6), partly vesicles with structured granular content (2, 5, 7). Both types show marked variations in size. In many cases the vesicle seems dilated, the nucleus being asymmetrical, so that on section signet-ring forms appear (2, 5) and anuclear vesicles (4). Only a very few granules (3) are of the same size and shape as specific granules in glomera.

Magnification: $\times 40,000$.

Fig. 9.5.

Secretory granules. Organ of Zuckerkandl cr 55.

All granules are bordered by vesicles, a few show structured content (3, 6), others a homogeneous content (1, 2, 4, 5, 7). Both types show marked variations in size.

Magnification: $\times 40,000$.

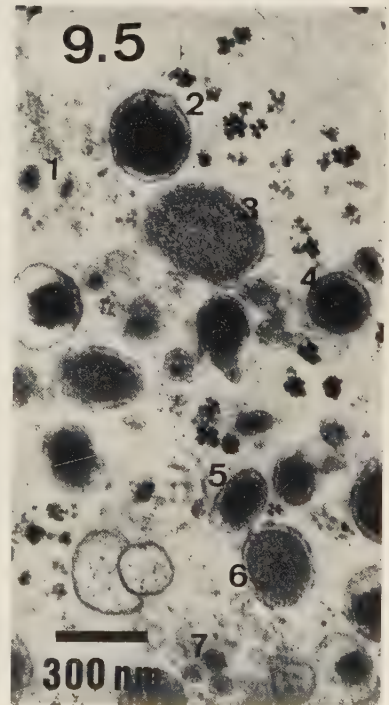
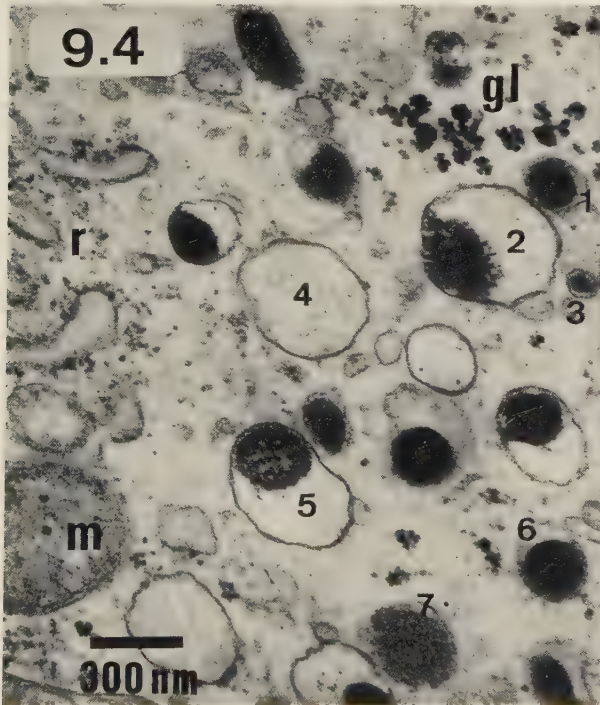
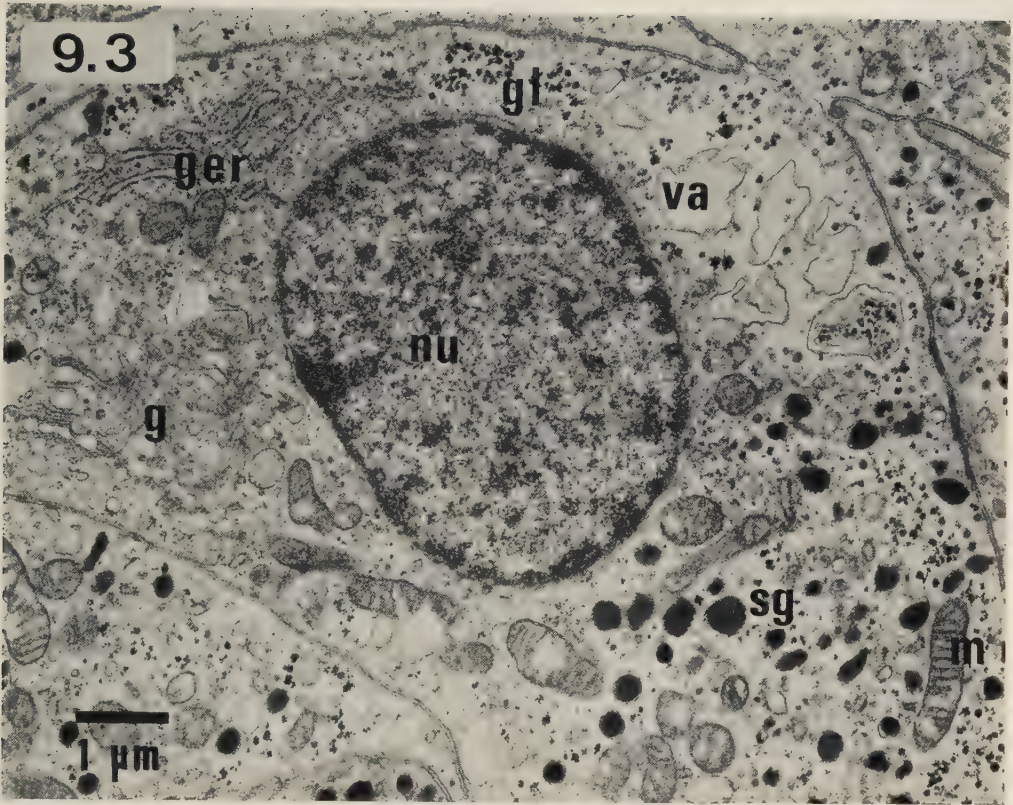


Fig. 9.6.

Light microscopic micrograph. Ganglion of sympathetic trunk cr 61, cf. Fig. 5.20.

The nuclei in the cells of the ganglion show very considerable variation in chromatin density. A number of cells exhibit the large, round, pale nucleus with one or more asymmetric nuclei characteristic of sympathetic ganglion cells (1), others show a somewhat denser chromatin structure, but may still be identified as ganglion cells (2, 3). Several cells have a considerably denser chromatin structure (4). Among the latter, some are satellite cells, whereas others have to be interpreted as sympathicoblasts considering their organelle content, cf. Fig. 9.7. The ganglion is sparsely vascularized. The nerve fibres are visible in the light microscope only when present in thick bundles (5).

Magnification: $\times 640$.

Fig. 9.7.

Electron microscopic low power view. Ganglion of sympathetic trunk cr 59.

Owing to the cytoplasmic content of ribosomes and specific granules (cf Figs. 9.8, 9.12) most of the cells may be characterized as ganglion cells (sympathicoblasts) at different stages of development, reflected in the chromatin structure of the nuclei. The chromatin is dispersed (gc_1), more condensed (gc_2 , gc_3), or in coarse, irregular fragments (gc_4). Among the cells with dark nuclei it is difficult, often impossible(?) to discern the neurolemmal cells (sw). A major area (nf_1) is predominated by nerve fibres which are also present in smaller quantities between and adjoining the perikarya of the cells (at nf_2).

Magnification: $\times 4,900$.

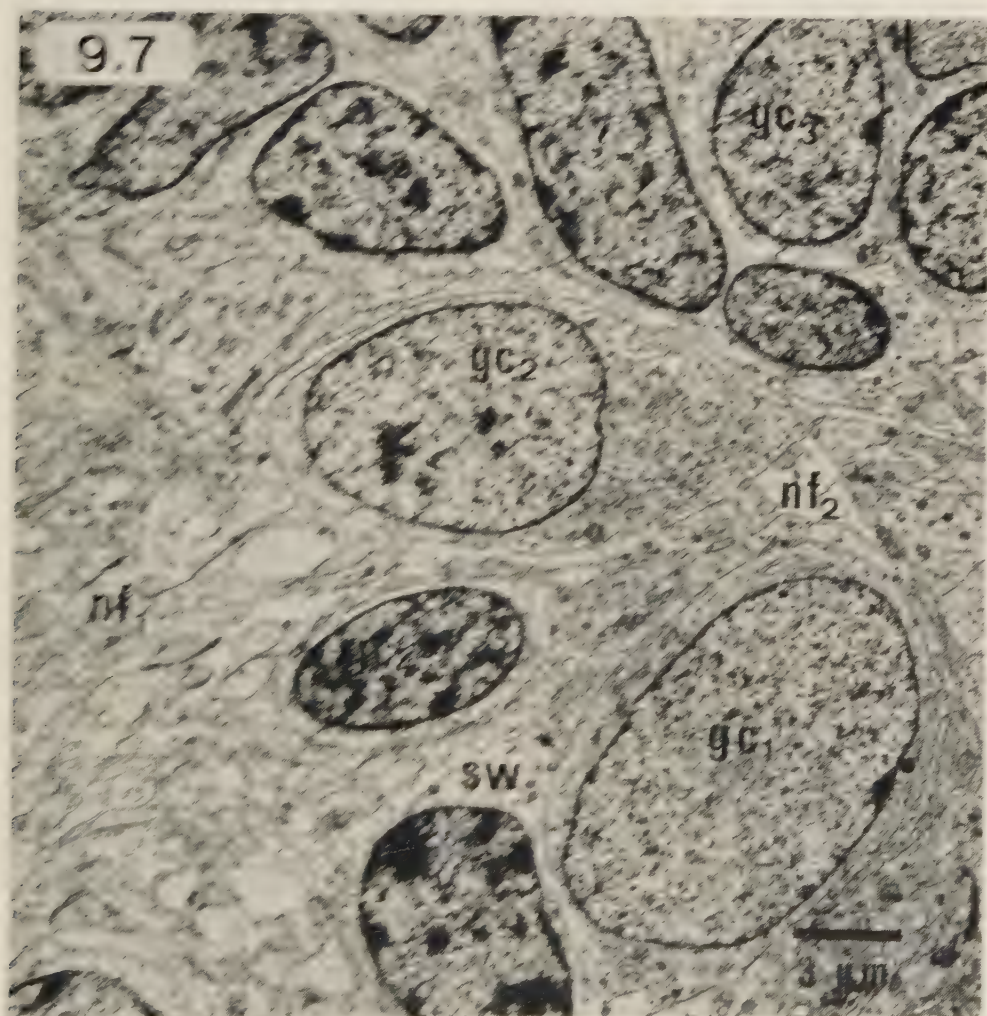
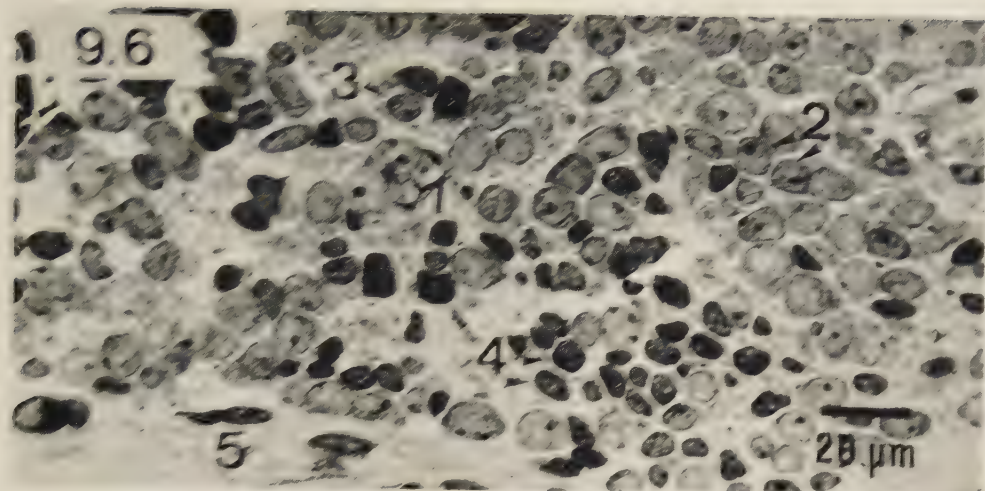


Fig. 9.8.

Ganglion cell. Ganglion of sympathetic trunk cr 61.

Owing to the chromatin structure of the nucleus (gc) the cell must be characterized as a developmentally intermediary type. The perikaryon is predominated by ribosomes which occur in large numbers as polyribosomes (r) or bound to the scattered vesicles and short cisterns of the endoplasmic reticulum (ger). Mitochondria (m) are few and small. In a neighbouring ganglion cell a Golgi zone (g). The areas at 9.9, 9.10, 9.11, and 9.12 are given in higher magnification in the named figures.

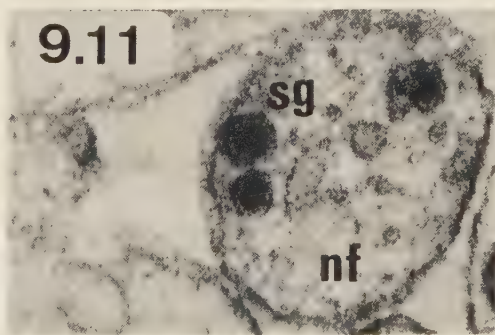
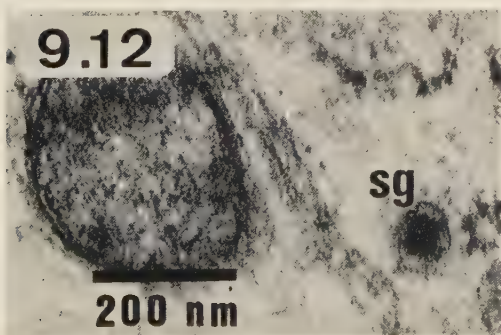
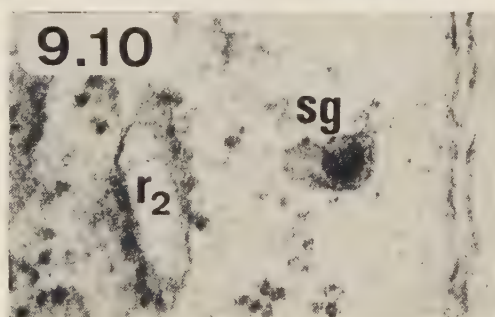
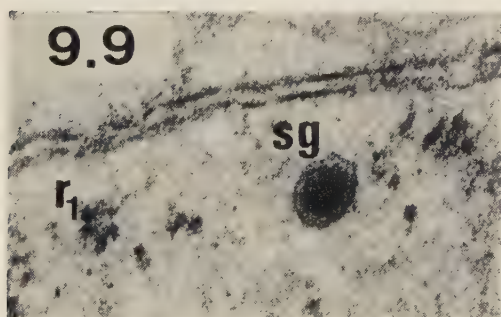
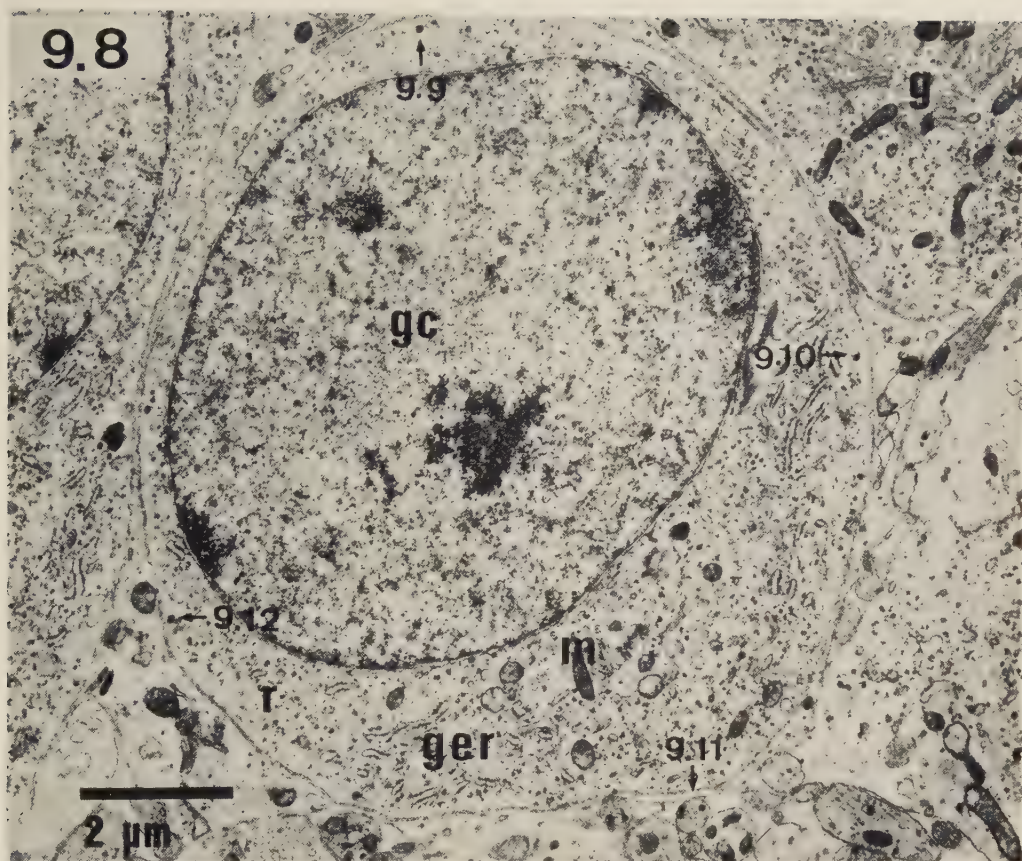
Magnification: $\times 9,500$.

Figs. 9.9, 9.10, 9.11, and 9.12.

Osmiophilic granules. Ganglion of sympathetic trunk cr 61.

High power views of the areas marked in Fig. 9.8. Specific granules (sg), microsome (r_2), polyribosome (r_1), nerve fibre with granules (nf). Nerve fibres containing granules must be assumed to be postganglionic adrenergic fibres from the cells of the ganglion, whereas the other nerve fibres are preganglionic cholinergic fibres to the cells of the ganglion (or postganglionic fibres which in the section concerned have not been cut through a granule).

Magnification: $\times 90,000$.



Statistical Analysis

Material and Method

For the measurement of the granules the author used a Zeiss particle size analyser TGZ-3. The apparatus was adjusted so as to record the frequency in 48 class intervals (the 44 largest ones being used) with linear correlation between the number of the class intervals and the diameter of the measuring mark (a spot of light).

The measurements were made on electron microscopic micrographs magnified so as to give a granular diameter of 3.42 mm (beginning point in the 5th class interval of the apparatus) to 27.71 mm (largest point in the 48th class interval of the apparatus). For each random sample measurements were made on micrographs of the same magnification. For measuring each granule the circular measuring mark of the apparatus was adjusted to the size which covered the area delimited by the vesicle of the granule concerned. As the granules were seldom circular, visual interpolation had to be employed.

In Table I (p. 296) the result of the measurements is given, stating the interval limits and the class interval midpoints of the apparatus, the number of granules having diameters in the class intervals for each of the 57 random samples, and the magnification of the micrographs.

In calculating parameters, the author used the class interval midpoint corrected for the magnification. The statistical analysis of the material was done by computer. A few calculations were checked by manual calculation on an electronic calculation machine.

The following statistical parameters and tests were used:

Mean value: $\bar{x} = \frac{x_1 + x_2 + \dots + x_n}{n}$, where $x_1, x_2, \dots, x_n$ are the diameters in n measured granules.

Variance: $s^2 = \frac{(x_1 - \bar{x})^2 + (x_2 - \bar{x})^2 + \dots + (x_n - \bar{x})^2}{n - 1}$

Standard deviation: $s = \sqrt{s^2}$

Standard error of the mean: $s_{\bar{x}} = \frac{s}{\sqrt{n}}$

95 % interval: $\bar{x} \pm 1.96 \times s.$

Chi-square test in comparing the observed distribution with the normal distribution:

$$\chi^2 = \sum \frac{(f - F)^2}{F}, \text{ where } f \text{ is the observed}$$

Table 1. Frequency table showing the result of the measurements of osmiophilic granules. For explanation, please consult text p. 295.

Interval limits, mm	Interval midpoint, mm	Carotid glomus cr 55, random sample 1	Carotid glomus cr 55, random sample 2	Carotid glomus cr 55, random sample 3	Carotid glomus cr 55, random sample 4	Inf. aorticopulmonary glomus cr 55	Middle aorticopulmonary glomus cr 55	Sup. aorticopulmonary glomus cr 55	Left subclavian glomus cr 55	Tympanojugular glomus cr 55	Vagal glomus cr 55a
3.42											
3.97	3.70	0	0	0	0	0	0	0	0	0	0
4.52	4.25	0	0	0	0	0	0	0	0	0	0
5.08	4.80	0	0	0	0	0	0	0	0	0	0
5.63	5.35	0	0	0	0	1	1	0	0	0	0
6.18	5.90	0	0	0	0	2	2	0	0	1	3
6.73	6.46	0	0	0	0	6	9	0	1	5	8
7.28	7.01	0	2	1	2	7	15	0	1	13	10
7.84	7.56	0	0	1	6	18	14	0	2	20	23
8.39	8.11	0	0	5	6	14	25	2	1	9	16
8.94	8.66	1	10	14	20	14	19	10	4	17	20
9.49	9.22	2	9	18	15	19	17	15	8	16	13
	9.77	8	13	15	16	9	4	6	9	2	7
10.04	10.32	7	18	13	8	9	4	15	7	4	4
10.60	10.87	10	25	5	7	3	0	13	13	7	1
11.15	11.42	12	9	10	5	2	0	9	12	3	1
11.70	11.98	14	9	3	3	1	0	14	9	2	0
12.25	12.53	16	6	6	5	1	1	10	8	1	0
12.80	13.08	12	2	1	0	0	1	4	6	0	1
13.36	13.63	8	1	0	0	0	1	4	4	2	0
13.91	14.18	9	2	1	1	0	0	2	2	1	1
14.46	14.74	7	0	1	1	0	0	1	5	0	0
15.01	15.29	4	0	1	0	0	0	0	2	0	1
15.56	15.84	5	2	0	0	0	0	2	1	1	0
16.12	16.39	3	0	0	0	0	0	1	2	0	0
16.67	16.94	1	1	0	0	0	0	0	1	0	0
17.22	17.50	0	0	0	0	0	0	0	1	0	0
17.77	18.05	1	0	0	0	0	0	0	0	0	0
18.32	18.60	0	0	0	0	0	0	0	0	0	0
18.88	19.15	2	0	0	0	0	0	0	1	0	0
19.43	19.70	0	0	0	0	0	0	0	0	0	0
19.98	20.26	0	0	0	0	0	0	0	0	0	0
20.53	20.81	0	0	0	0	0	0	0	0	0	0
21.08	21.36	0	0	0	0	0	0	0	0	0	0
21.64	21.91	0	0	0	0	0	0	0	0	0	0
22.19	22.46	0	0	0	0	0	0	0	0	0	0
22.74	23.02	0	0	0	0	0	0	0	0	0	0
23.29	23.57	0	0	0	0	0	0	0	0	0	0
23.84	24.12	0	0	0	0	0	0	0	0	0	0
24.40	24.67	0	0	0	0	0	0	0	0	0	0
24.95	25.22	0	0	0	0	0	0	0	0	0	0
25.50	25.78	0	0	0	0	0	0	0	0	0	0
26.05	26.33	0	0	0	0	0	0	0	0	0	0
26.60	26.88	0	0	0	0	0	0	0	0	0	0
27.16	27.43	0	0	0	0	0	0	0	0	0	0
27.71											
Total		122	109	95	95	106	113	108	100	104	109
Magnification /10 ³		114	90	90	90	70	70	96	114	70	74

Interval limits, mm	Interval midpoint, mm	Vagal glomus cr 59a	Vagal glomus cr 59b	Sympathetic ganglia cr 59	Organ of Zucker- kandl cr 59	Carotid glomus cr 61, random sample 1	Carotid glomus cr 61, random sample 3	Carotid glomus cr 61, random sample 4	Inf. aorticopulmonary glomus cr 61a	Inf. aorticopulmonary glomus cr 61b	Middle aorticopulmonary glomus cr 61a	Middle aorticopulmonary glomus cr 61b	Sup. aorticopulmonary glomus cr 61	Left subclavian glomus cr 61	Sympathetic ganglia cr 61	Organ of Zucker- kandl cr 61	Carotid glomus cr 62, random sample 1
3.42	3.70	0	0	0	1	0	0	0	0	0	0	0	0	0	0	2	0
3.97	4.25	0	0	0	3	0	0	0	0	0	0	0	0	0	0	6	0
4.52	4.80	0	0	0	4	0	0	0	0	0	0	0	0	0	0	5	0
5.08	5.35	0	0	0	2	0	0	0	0	0	0	0	0	0	0	3	0
5.63	5.90	0	0	0	4	0	0	0	0	0	0	0	0	0	0	7	0
6.18	6.46	0	0	0	1	0	0	0	0	0	0	0	0	0	0	3	0
6.73	7.01	0	0	0	2	0	0	0	0	0	0	1	0	0	0	4	0
7.28	7.56	0	0	0	3	1	0	1	1	0	0	1	1	0	0	4	0
7.84	8.11	0	0	0	6	0	2	5	1	2	1	3	1	0	0	1	0
8.39	8.66	3	0	0	0	7	1	4	2	1	2	1	1	0	0	6	0
8.94	9.22	1	0	0	1	4	12	19	6	3	1	9	2	0	0	5	0
9.49	9.77	4	4	0	11	9	14	8	12	3	2	11	3	0	0	9	3
10.04	10.32	3	3	0	1	15	11	17	8	3	1	16	8	6	0	9	6
10.60	10.87	14	6	0	7	14	8	6	16	9	8	7	5	6	0	6	10
11.15	11.42	8	6	0	10	14	9	9	15	13	5	7	4	9	1	12	17
11.70	11.98	13	10	1	7	19	6	6	13	20	14	13	12	7	0	13	14
12.25	12.53	10	18	0	3	10	8	7	7	15	6	7	8	11	0	12	19
12.80	13.08	13	12	0	9	6	7	6	5	12	8	2	5	8	1	11	22
13.36	13.63	11	13	0	4	7	3	3	9	20	17	3	12	19	2	10	11
13.91	14.18	9	14	0	6	3	8	1	6	15	7	6	13	6	3	14	15
14.46	14.74	7	6	1	10	2	1	0	1	10	11	4	11	10	6	15	7
15.01	15.29	1	4	1	7	1	3	3	1	9	5	2	5	5	5	11	11
15.56	15.84	2	3	1	3	1	4	0	2	9	2	1	5	9	8	4	6
16.12	16.39	4	2	6	3	0	1	0	0	6	4	2	5	2	5	5	1
16.67	16.94	3	1	7	10	1	0	4	0	6	0	2	6	0	10	2	1
17.22	17.50	0	0	9	7	0	2	1	1	2	4	1	3	2	11	5	0
17.77	18.05	0	2	8	9	0	1	0	0	1	1	1	1	1	9	3	0
18.32	18.60	0	1	6	6	0	0	1	0	3	0	2	1	0	15	4	2
18.88	19.15	1	1	13	6	0	0	0	0	0	0	0	0	0	6	4	0
19.43	19.70	0	0	10	4	0	0	0	0	2	0	0	1	0	6	1	0
19.98	20.26	0	0	8	5	0	0	0	0	0	0	0	0	0	4	1	0
20.53	20.81	0	0	9	4	0	0	0	0	0	0	0	0	0	6	1	0
21.08	21.36	0	0	4	4	0	0	0	0	0	0	0	0	0	2	1	0
21.64	21.91	0	0	3	1	0	0	0	0	0	0	0	0	0	4	1	0
22.19	22.46	0	0	1	0	0	0	0	0	0	0	0	0	0	3	0	0
22.74	23.02	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0
23.29	23.57	0	0	4	1	0	0	0	0	0	0	0	0	0	3	0	0
23.84	24.12	0	0	1	0	0	0	0	0	0	0	0	0	0	2	1	0
24.40	24.67	0	0	1	1	0	0	0	0	0	0	0	0	0	2	1	0
24.95	25.22	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
25.50	25.78	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
26.05	26.33	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
26.60	26.88	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
27.16	27.43	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
27.71		0	0	0	0	0	0	0	0	0	0	0	0	0	0	4	0
Total		107	106	98	168	114	101	101	106	164	99	102	113	101	114	206	145
Magnification /10 ³		114	114	238	56	102	102	102	90	114	114	114	114	114	238	60	114

[illegible]

number and F the number expected at a normal distribution in each of 12 cells. Significance limits at 5 degrees of freedom read from Documenta Geigy, p. 36.

F test on comparison of the variances of two random samples:

$$F = \frac{s_a^2}{s_b^2}$$

with degrees of freedom $n_a - 1$, $n_b - 1$, where s_a and s_b are the standard deviation ($s_a > s_b$) and n_a and n_b the number of observations in the two compared random samples a and b . Significance limits read from Documenta Geigy, pp. 40-41.

t test in comparing the mean values of two random samples:

$$t = \frac{\bar{x}_a - \bar{x}_b}{\sqrt{\frac{s_a^2}{n_a} + \frac{s_b^2}{n_b}}} \quad \text{with degrees of freedom} \quad \frac{\left(\frac{s_a^2}{n_a} + \frac{s_b^2}{n_b}\right)^2}{\frac{\left(\frac{s_a^2}{n_a}\right)^2}{n_a + 1} + \frac{\left(\frac{s_b^2}{n_b}\right)^2}{n_b + 1}} 2^{-2}$$

where $\bar{x}_a$ and $\bar{x}_b$ are mean values, s_a and s_b standard deviation, and n_a and n_b number in the two compared random samples a and b . Significance limits read from Documenta Geigy, pp. 32-35.

Variance analysis in comparing mean values: According to Croxton, pp. 295-300. Significance limits for F distribution read from Documenta Geigy, pp. 40-41.

Results

The vesicular diameters of the osmiophilic granules are listed in Table II (p. 302) which sets out the number of measured granules, the mean, standard deviation, and standard error of the mean for each of 15 random samples from the carotid glomera, 1 random sample from each of the 34 microscopic glomera subjected to electron microscopy, 1 random sample from sympathetic ganglion cells from each foetus, and 1 random sample from chromaffin cells in the organ of Zuckerkandl from each foetus.

The chi-square test of the distribution of each of these 57 random samples showed that they did not differ from a normal distribution (tympanojugular glomus cr 55: $P = 0.05 - 0.01$, all other random samples from glomera, ganglion cells, and chromaffin cells: $P > 0.05$).

If granules from the carotid glomera and the microscopic glomera are derived from the same population, the mean and variance would be expected to be equal, apart from differences that are due to chance. This hypothesis was tested by paired comparison of the random samples from the microscopic glomera with the random samples from the carotid glomera in a two-sided F and t tests (in the t test there was not a presupposition of variance equality). At a 5 % significance level it could not be ruled out on this basis that each random sample from microscopic glomera was derived from the same population as one or more of the random samples from the carotid glomus. (Exceptions are the tympanojugular glomus cr 55 (highest $P_t = 0.05 - 0.01$) and the inferior aorticopulmonary glomus cr 61a (highest $P_t < 0.01$). An example of P values is given in Table II). However, there were in all cases significant differences between each of the random samples from microscopic glomera and one or more random samples from the carotid glomera. By paired comparison of the 15 random samples from the carotid glomera using the F and t test with a 5 % significance level, differences in variance were found in 1/3 (34.3 %) and differences in mean values in 2/3 (61.0 %) of the tests. Presupposing that granules from the carotid glomera belong to the same population, the F and t tests in the present material demonstrated non-existent differences in variance and mean value. At variance analysis of the random samples from the carotid glomera there was a greater variation between the random samples than what could reasonably be explained by the variation within the random samples. This applied at the 5 % significance level to the difference between all the random samples from the carotid glomera, to the difference between the random samples from the carotid glomus in the same foetus (except the random samples from the carotid glomus of foetus cr 61: $P > 0.05$), and to the difference between the random samples from the right and left carotid glomus from the same foetus. Variance analysis of random samples from identical micrographs (two measurements of the same granules) revealed no notable difference (carotid glomus cr 55, cr 59, and cr 62: $P > 0.05$; carotid glomus cr 61: $P = 0.05 - 0.01$). Thus, the demonstrated, non-expected differences between the random samples from the carotid glomera cannot be explained by inaccuracy of the measurements. Presumably they are due to a considerable inaccuracy of the magnification of the micrographs owing to the adjustment of the electron microscope and the photographic enlargement not being exact. The inaccuracy of the magnification is estimated to be $\pm 10\%$. If this inaccuracy is included in the assessment, it cannot be excluded in the statistical analysis that the random samples from the microscopic glomera and from the carotid glomera are derived from the same population.

If granules from the chromaffin cells and the glomera are derived from the same population, the mean and variance would be expected to be equal, apart from differences that are due to chance. In the t and F tests (two-sided tests; in the t test variance equality was not presupposed) there was, at a significance level of 1 %, a difference between the random samples on paired comparison

Foetus cr 61															
Glomus 1	{	P _F	P _t	{	xx	xxx	xx	xxx	xxx	xx	xx	xxx	xx	xx	
					xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	
					xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	
					xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	
Sympathetic	{	P _F	P _t	{	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx		
					xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	
					xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	
					xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	
Chromaffin	{	P _F	P _t	{	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx		
					xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	
					xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	
					xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	
Number					114	101	101	106	164	99	102	113	101	114	206
Mean, nm					112	115	109	129	118	116	103	118	117	77	210
Standard deviation					16	22	23	20	20	18	22	21	16	11	77
Standard error of the mean					1.5	2.2	2.2	1.9	1.5	1.8	2.2	2.0	1.6	1.1	5.4
Glomus 1	{	P _F	P _t	{	xx	xx	x	xxx	xxx	x	xxx	xxx	x		
					xxx	xx	x	xxx	xx	xxx	xx	xx			
					xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx			
					xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx			
Sympathetic	{	P _F	P _t	{	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx		
					xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx			
					xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx			
					xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx			
Chromaffin	{	P _F	P _t	{	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx		
					xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx			
					xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx			
					xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx			

[illegible]

of each of the random samples from chromaffin cells with each of the random samples from glomera. On this basis it is concluded that the granules from the two cell types are not derived from the same population.

If granules from the sympathetic cells and the glomera are derived from the same population, the mean and variance would be expected to be equal, apart from differences that are due to chance. At the *t* and *F* tests (two-sided tests; in the *t* test an equality of variance was not presupposed) there was, at the 1 % significance level, a difference between the random samples on paired comparison of each of the 4 random samples from sympathetic ganglion cells with each of the random samples from microscopic glomera (except in comparing the variances for sympathetic ganglion cells from the foetus with a crown-rump length of 62 mm and the left subclavian glomus cr 61, $P = 0.05-0.01$). On this basis it is concluded that the granules from the two cell types are not derived from the same population.

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The figures in brackets refer to the pages in the present volume on which the respective publication is quoted. Pages in quoted books are marked p. Names of periodicals abbreviated in accordance with World Medical Periodicals (H. A. Clegg: World Medical Association, 3rd edition 1961 and supplement 1968). Names of periodicals not adopted in this list are given unabbreviated.

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Appendix IV

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Errata

- Preface, 6th line from bottom: surgeon, and read surgeon,
- Preface, 3rd line from bottom: Library, read Library, and
- Preface, bottom line: heartfelt read heartfelt
- p. 10, bottom line: xxx read 324
- p. 11, 2nd line from bottom, diameters read diameters
- p. 311, 5th line from top: delete: the innervation of

